
**“TO STUDY HNC-LL AS A POTENTIAL SCORE
FOR PREDICTING SEVERITY IN COVID-19
PATIENTS - A ONE YEAR HOSPITAL BASED
CROSS SECTIONAL STUDY IN KLES
Dr.PRABHAKAR KORE HOSPITAL AND MEDICAL
RESEARCH CENTRE, BELAGAVI.”**

BY

REG NO: BG0120004

Dissertation

Submitted to

KAHER, Belagavi, Karnataka,

In partial fulfilment of the requirements for the degree of

M.D.

IN

GENERAL MEDICINE

**DEPARTMENT OF GENERAL MEDICINE
JAWAHARLAL NEHRU MEDICAL COLLEGE,
KAHER, BELAGAVI – 590010
KARNATAKA.**

JUNE/JULY 2023

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DR. REKHA S PATIL MD
Professor and Head,
Department of General Medicine,
J. N. Medical College,
Nehru Nagar, Belagavi – 10

Date : 31/12/2022
Place : Belagavi



DR.(Mrs.) N.S. MAHANTSHETTI MD
Principal
PRINCIPAL
J.N. Medical College,
BELAGAVI- 590 010
J. N. Medical College,
Nehru Nagar, Belagavi – 10

Date : 02/01/2023
Place : Belagavi

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Placed in Category 'A' by MHRD (GoI)



0831 - 2471350

Nehru Nagar, Belagavi- 590 010, Karnataka, INDIA



0831 - 2470759



www.jnmc.edu

principal@jnmc.edu

Ref No: MDC/PG/

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Dr. (Mrs.) N.S. Mahantashetti,
Chairperson-Antiplagiarism Committee &
Principal,
J. N. Medical College, Belagavi.

To,
Reg. No. BG0120004,
Postgraduate Student,
2020-21 Batch,
Department of General Medicine,
J. N. Medical College, Belagavi.

ETHICAL CLEARANCE LETTER



K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
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Accredited 'A' Grade by NAAC (2nd Cycle)

Placed in Category 'A' by MHRD (GoI)

**JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)**

Website: <http://www.jnmc.edu>
E-Mail : dome@jnmc.edu

Phone: (+ 91-(0)831 Office : 2472550
Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref: MDC/DOME/ 24

Date: 25/01/2021

To,

REG NO: BG0120004

PG student in Medicine,
J.N.Medical College,
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled “TO STUDY HNC-LL AS A POTENTIAL SCORE FOR PREDICTING SEVERITY IN COVID-19 PATIENTS – A ONE YEAR CROSS SECTIONAL STUDY AT A TERTIARY CARE HOSPITAL”, is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. Smita Sonoli)
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

(Dr. Harsha Hegde)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

ABBREVIATIONS

ANC	–	Absolute neutrophil count
ALC	–	Absolute leucocyte count
apTT	–	Activated partial thromboplastin time
ARDS	–	Acute Respiratory Distress Syndrome
BNP	–	Brain Natriuretic Peptide
CAP	–	Community Acquired Pneumonia
CK	–	Creatinine Kinase
CFR	–	Case fatality rate
CURB-65	–	Confusion, Urea, Respiratory Rate, Blood pressure, Age>65
CRP	–	C - Reactive Protein
CT	–	Computed Topography
hACE	–	Human angiotensin converting enzyme
HNC-LL	–	Hypertension, neutrophil, C-reactive protein, LDH, Lymphocyte count
ICU	–	Intensive care unit
INR	–	International Normalised Ratio
IFN	–	Interferon
IL	–	Interleukin
LDH	–	Lactate Dehydrogenase
MuLBSTA	–	Multilobar infiltrate, Lymphocyte count, Bacterial infection, Smoking history, Hypertension and Age
NLR	–	Neutrophil to Lymphocyte Ratio
NSP	–	Non structural proteins
ORFS	–	Open Reading Frame

PCT	–	Procalcitonin
PSI	–	Pneumonia Severity Index
PT	–	Prothrombin time
qSOFA	–	Quick SOFA
RAT	–	Rapid Antigen test
RNA	–	Ribonucleic acid
RR	–	Respiratory Rate
RTPCR	–	Reverse transcription polymerase chain reaction
SARS CoV-2	–	Severe Acute Respiratory Syndrome Corona Virus 2
SGOT/ AST	–	Serum Glutamic oxaloacetic acid transaminases
SGPT/ ALT	–	Serum Glutamic-pyruvic transaminases
SMD	–	Standard Mean Difference
SOFA	–	Sequential Organ Failure Assessment
SpO ₂	–	Oxygen Saturation
TGF	–	Transforming Growth Factor
t-PA	–	Tissue plasminogen activator
TNF	–	Tumor Necrosis Factor
VEGF	–	Vascular endothelial growth factor

ABSTRACT

BACKGROUND:

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is associated with significant morbidity and mortality. The aim of the present study was to evaluate the role of HNC-LL score as an early predictor of COVID-19 severity and to further compare its effectiveness with known scores such as CURB-65, MuLBSTA, Neutrophil to Lymphocyte ratio.

METHODS

In the present observational study, 142 adult patients with a confirmed diagnosis of COVID-19 admitted to KLES Dr. Prabhakar Kore Hospital Between 01 October 2020 to 30 December 2021 were included. Patients' demographics, symptoms, history, respiratory rate and oxygen saturation levels were recorded. Based on haematological, inflammatory, coagulation and biochemical markers, disease severity indexes including CURB-65, MuLBSTA, NLR and HNC-LL were calculated.

Results

The study population comprised of 78.17% males, Mean \pm standard deviation (SD) age of 55.67 ± 15.63 years. The mean duration of hospital stay was significant in improved vs expired patients (10.58 ± 7.43 days Vs 6.96 ± 4.9 days; $p=0.0024$). The median NL ratio (9.67 vs 8.58 ; $p=0.3241$), HNC-LL score (2 vs 1 ; $p=0.3124$), CURB-65 (2 vs 2 ; $p=0.7562$) and MuLBSTA (3 vs 3 ; $p=0.0632$) between expired and improved groups were comparable. Overall, there was significant positive correlation between HNC-LL & NL ratio, HNC-LL & MuLBSTA, NL ratio & MuLBSTA and NL ratio & CURB-65 ($p<0.05$). Similarly, we observed a significant difference in

distribution of NL ratio ($p=0.0011$), HNC-LL ($p=0.0123$) and CURB-65 ($p<0.001$) with the severity of disease. The AUC for HNC-LL score is 0.75(95% CI: 0.534-0.760) at cut-off > 2.5 .

Conclusion

Based on the results of our study, novel scoring system like HNC-LL can be considered a predictive marker of COVID-19 severity and outcome. Early identification of patients with severe COVID-19 followed by early interventions are beneficial in saving lives.

Keywords: COVID-19, HNC-LL, screening, early diagnosis disease severity, outcome

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INTRODUCTION

From the first reported case of Coronavirus disease 2019 (COVID-19) at Wuhan in December 2019, is caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). It has evolved rapidly into a pandemic affecting over 608 million people around the world. More than 6.5 million deaths are reported till date in this pandemic¹. The increased risk of transmission of the SARS-CoV-2 virus is responsible for the quick rise in new cases and the disease's spread. Based on the severity in clinical manifestations, pulmonary function tests, and radiological findings, the disease is categorized as mild, moderate and severe.²

Due to rapid progression and poor prognosis of severe cases, identification of early clinical and laboratory parameters that can predict the progression of disease are paramount. This will allow for the stratification of patients who may have severe COVID-19 and a high mortality rate, and it will also further guide streamlining the management protocols based on severity, lowering the mortality rate, increasing the survival rate, and lowering the burden for the healthcare system.³

Severe disease is characterised by increased respiratory rate $>30/\text{min}$, decreased $\text{SpO}_2 <93\%$ at rest, in respiratory failure, shock, end organ damage necessitating intensive care and mechanical ventilation³. Additionally, changes in the laboratory parameters including hematological, coagulation and biochemical parameters are found to be beneficial in grading severity of COVID-19⁴⁻⁷.

Several predictive markers are being used to predict the severity of disease. They include CURB-65 (Confusion, Urea levels $>7\text{mmol/L}$, Respiratory rate ≥ 30 cycles/min, Blood pressure $<90/60\text{mmHg}$ and age >65 years)⁸ that estimates mortality

of CAP to determine inpatient vs outpatient treatment, MuLBSTA (Multilobe infiltrate, Absolute Lymphocyte count $<0.8 \times 10^9/L$, Bacterial infection, Smoking history, Hypertension and Age <60 years) that predicts 90 day mortality in patients with viral pneumonia⁹, Neutrophil to Lymphocyte Ratio (NLR; normal range: 0.78 to 3.53) is a marker of subclinical inflammation and is used to differentiate simple viral syndrome from bacteremia or sepsis and also as a prognostic marker in cardiovascular disease and cancer¹⁰.

HNC-LL (Hypertension $>140/90$ mmHg, Neutrophil count $>6.3 \times 10^9/L$, C-Reactive protein >10 mg/L, Lymphocyte count $<1.1 \times 10^9/L$ and Lactate dehydrogenase levels >245 U/L) is a new scoring method specific for COVID-19 disease to accurately distinguish patients with high and low risk of disease in the early stage.¹¹

Although initially the virus was implicated as a respiratory pathogen, several researches have indicated its pathogenicity across multiple systems including cardiovascular, gastrointestinal, neurological, hematopoietic and immunological systems^{12,13}. Therefore, with diversity of disease spectrum with clinical features laboratory investigation, radiological investigations and prognosis, identifying the patients at risk of severe disease at the early disease stages is paramount. Collective data from the pre-existing disease severity scores and novel scores will be beneficial in assessing the disease severity, prognosis and post COVID comorbidities.

In view of this, the present study was planned to comparatively evaluate the role of novel HNCLL score as a predictive marker of COVID-19 severity.

AIM AND OBJECTIVES

AIM

To evaluate the role of HNC-LL score as an early predictor of COVID-19 severity and to further compare its effectiveness with known predictors such as CURB-65, MuLBSTA, Neutrophil to Lymphocyte ratio.

OBJECTIVES

- To evaluate the role of HNC-LL score in early prediction of severity in COVID-19 patients.
- To compare HNC-LL score with CURB-65, MuLBSTA, Neutrophil to Lymphocyte ratio in predicting COVID-19 severity

REVIEW OF LITERATURE

Following the Spanish flu pandemic that happened over a century ago, the current coronavirus disease 2019 (COVID-19) is the fifth pandemic affecting people worldwide¹⁴. While most of the pandemics were caused by influenza virus, the COVID-19 is caused by the novel virus severe acute respiratory syndrome-coronavirus (SARS-CoV-2). The previous decade had witnessed other virus outbreaks of the coronavirus family including the SARS and Middle East Respiratory Syndrome having fatality rates of 9.5% and 34.4%, respectively¹⁵.

History and Epidemiology of COVID-19

A number of pneumonia cases with a significant mortality rate were reported in December 2019 in Wuhan city, Hubei province. The discovery of beta-corona virus in lower respiratory sample analysis led to the identification of 2019 novel corona virus (2019 n CoV)¹⁶. Further study revealed that the virus was comparable to coronavirus strains obtained from bats, and on February 11, 2020, the International Committee on Taxonomy of Viruses designated the virus as SARS-CoV2 based on phylogeny and taxonomy.¹⁷ The associated illness was referred to as Coronavirus disease (COVID-19), and on 11 March 2020, the World Health Organization classified COVID-19 to be a global pandemic¹⁸.

The first COVID-19 case in India was detected on March 12, 2020. The virus spread quickly, and within a month, there were 10,000 cases nationwide¹⁹. COVID-19 had spread rapidly globally and as of 07 October 2022, WHO reports 617,597,680 confirmed COVID-19 cases and 6,532,705 deaths due to COVID-19 globally and 44,606,460 confirmed cases of COVID-19 including 5,28,754 reported

deaths in India¹. Although the current infectivity rate is controlled due to ongoing vaccination programs, the country is still witnessing the occurrence of new cases and deaths even today.

Structure of SARS-CoV2

Coronaviruses are RNA viruses, that belong to the order Nidovirales, family Coronaviridae and subfamily Coronavirinae. Based on genomic structure, Coronavirinae can be either alpha coronavirus, beta coronavirus, gamma corona virus or delta corona virus. The characteristic feature of these viruses is that they have a large genome, are replicative, exhibit unique enzymatic activities and have extensive ribosomal frameshifting¹⁹.

Coronavirus are enveloped in a positive single stranded RNA virus with genomes of 8.4 to 12kDa in size. The genomes of coronaviruses range are in size from 8.4 to 12 kDa. The viral genomes contain five structural proteins: the spike protein (S), membrane protein (M), nucleocapsid protein (N), envelope protein (E), and haemagglutinin-esterase protein. The major 5' terminal of the viral genome contains open reading frames encoding the proteins necessary for viral replication (HE)^{20,21}. The structure of coronavirus is depicted in Figure 1.

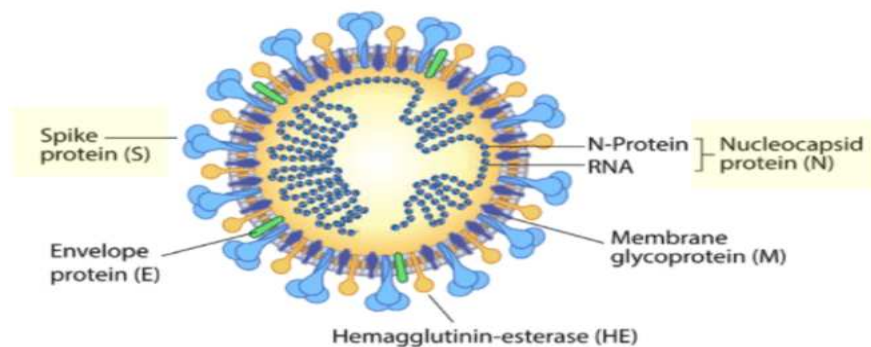


Figure 1: Structure of Coronavirus

Replication and pathogenesis of SARS-CoV-2

Replication of SARS-CoV-2 virus is depicted in Figure 2. Spike proteins attach to a particular cell surface receptor, such as a human angiotensin-converting enzyme (hACE), thus the coronavirus enters host cells. Upon entry there is uncoating of virus which allows the entry of viral genomic mRNA into the host cell cytoplasm. The ORFs get translated to polypeptides which give rise to NSPs which take part in replication and transcription processes. The completely replicated virus is then released out by exocytosis²².

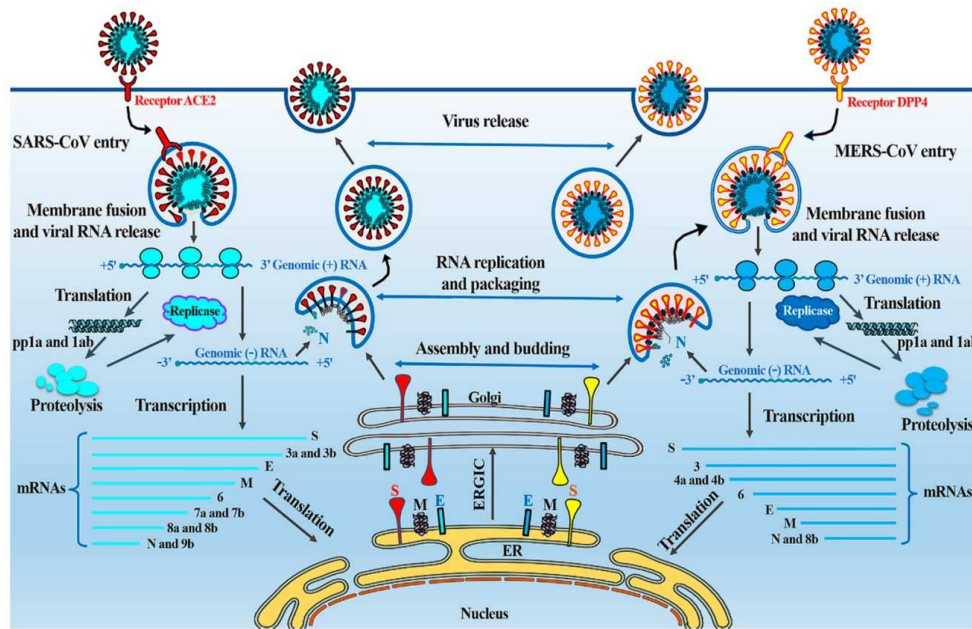


Figure 2: Replication of coronavirus

Pathogenesis of COVID-19 is not well understood. Literature suggests that S1 subunit of spike protein binds to the hACE2 receptor, which causes these receptors to be downregulated later and increases angiotensin II production. This increases the pulmonary vascular permeability resulting in lung injury. Antigen presenting cells on the virus also adhere to dendritic cells, where they activate macrophages. This causes

a strong immunological reaction that is characterized by high levels of chemokines (CCL5, CCL2, CCL3, CXCL9, CXCL8, CXCL10) and pro-inflammatory cytokines (IFN- α , IFN- γ , TNF- α , IL-1 β , IL-6, IL-18, IL-12, IL-33, TGF β , etc.) known as a "cytokines storm". These may reach the blood circulation and lead to multiorgan damage^{23,24}. Pathophysiology of SARS-CoV-2 is briefly summarized in Figure 3²⁵.

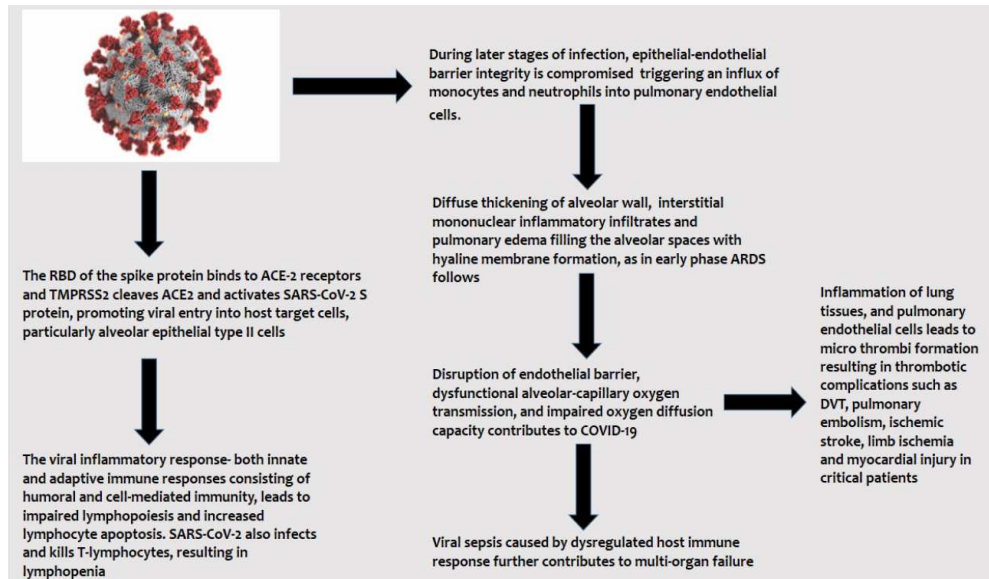


Figure 3: Pathophysiology of SARS-CoV-2

Transmission, Incubation period and infectivity period

Although initially it was believed to be of zoonotic origin and spread due to exposure to wet markets in China, the rapid spread across healthcare workers and across the world suggested a person to person spread. However, the exact mechanism was not elucidated. As the virus is primarily a respiratory pathogen the transmission was considered airborne or through direct or indirect contact of droplets from the infected person. Sources of viral spread include coughing, sneezing, droplet inhalation, contact with ocular, nasal, oral and mucosa^{27, 28}.

According to previous studies, the mean incubation period ranges between 5 to 6 days. Most infected patients remain asymptomatic and others develop symptoms as early as 2.2 days or within 11 days.²⁹ Although the duration for which the infected patient remains infective and risk is not very clear, however, studies suggest that viral load of oropharyngeal secretions are highest during early symptomatic disease and will decrease overtime. Evidence suggests that viral shedding in patients continue to occur even after resolution of symptoms and even for more than 4 weeks after negative test results for COVID-19 infection. Moreover, the possibility of transmission from asymptomatic patients is yet another reason for rapid spread of infection across masses.^{30, 31}

Clinical features

The COVID-19 disease spectrum ranges from asymptomatic to critical disease. Fever is the most common clinical manifestation. Other features include, dry cough, myalgia, dyspnea, diarrhea, abdominal pain, vomiting/nausea. Anosmia or hyposmia and loss of taste are typical features of COVID-19 and was seen in approximately 80% of patients. Absence of pneumonia or presence of mild pneumonia are categorized as mild disease. Presence of pneumonia along with dyspnea, low blood saturation level of <93%, respiratory frequency of >30/ min is considered as severe disease which needs hospitalization and ICU admissions. Patients with acute respiratory distress syndrome, arrhythmia, shock with or without multiorgan failure are categorized as critical patients^{32,33}.

Radiological findings

Radio imaging results differ based on age, disease severity, immune competency and drug therapy protocols. Computed tomography is recommended as an initial modality to assess disease severity. The hallmark of COVID-19 is multiple, bilateral, posterior and peripheral ground glass opacities on chest CT. In severe cases these are accompanied by infiltrating shadows²⁶.

Classification of disease severity is shown in Table 1 below:

Table 1: Stages/Severity of COVID-19 disease

Severity	Symptoms	Signs/ findings
Mild	Fatigue, myalgia, cough, fever	<ul style="list-style-type: none"> • Pneumonia Absent • SpO2: 95–98%
Moderate	Cough, fatigue, fever	<ul style="list-style-type: none"> • Unilateral, lobar pneumonia, • SpO2: 93–95 % • RR: >24 breath/min,
Severe (SARS)	Cough, dyspnea, fever, tachypnea	<ul style="list-style-type: none"> • Hypoxemic Acute respiratory failure: SpO2 < 93%, • RR: >30 breath/min • CT: 50 % bilateral pneumonia
Critical (SARS-ARDS)	Severe dyspnea et tachypnea, severe hypoxemia	<ul style="list-style-type: none"> • Acute respiratory failure –ARDS, • CT: >75 % bilateral pneumonia • mechanical ventilation, • Shock • Multiorgan dysfunction syndrome

Laboratory findings of COVID-19

- Hematological parameters include decreased platelet count, lymphocyte count, hemoglobin, eosinophil count and basophil count; and elevated neutrophil and neutrophil lymphocyte ratio³⁵.
- Inflammatory markers include elevated C-Reactive Protein, Erythrocyte Sedimentation Rate, Serum Ferritin, D-dimer, Lactate dehydrogenase, elevated levels of troponin and brain natriuretic peptide (BNP). High levels of cytokines and chemokines including IL6, IL-8, IL-9, IL-10, G-CSF, GM-CSF, TNF- α and VEGF.^{36,37}
- Coagulation markers include, increased levels of thrombin-antithrombin complex, α 2-plasmininhibitor-plasmin Complex, thrombomodulin t-PA/PAI-1 complex, prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin time (APTT), D-dimer, fibrinogen and thrombin time (TT).³⁸
- Biochemical markers include increased levels of creatine kinase, myoglobin, aspartate aminotransferase and alanine aminotransferase, procalcitonin, reduced albumin-globulin ratio, lactate dehydrogenase, glycosuria, proteinuria, and Creatine phosphokinase levels.²⁶

Predictive tools for disease severity

The assessment of community acquired pneumonia using recognized severity scores aids in better management. Below are the few commonly used scoring systems.

Pneumonia Severity Index (PSI)

PSI was the first scoring system. It consists of 20 clinical and laboratory parameters. Using these points, the patients can be assigned into 5 classes of risk. As the scoring system is complicated, it may not be feasible during emergency hospitalizations, therefore, other easier scoring system were formulated³⁹.

Neutrophil Lymphocyte ratio

NLR is a simple, readily available and reliable parameter to evaluate the immune inflammatory response, neuroendocrine stress and severity of illness. Although it is highly sensitive hematologic parameter, the specificity is less. Apart from immune inflammatory response, NLR is also helps evaluate relationship between brain and immune system.⁴⁰ Neutrophils and lymphocytes are activated by sympathetic and parasympathetic hormones, respectively suggesting increased circulating neutrophil count and decreased lymphocytes counts.⁴¹ The normal NLR in adults ranges from 1.0 to 2.3. The values <0.7 and >3.0 are considered pathological.⁴² A study by Song et al., determined 5.87 as the cut off value of NLR as a warning score of COVID-19 severity.⁴³

MuLBSTA

This is an early warning model for predicting severity and mortality in patients with viral pneumonia caused by influenza virus, adenovirus, bocavirus, human rhinovirus, parainfluenza virus, coronavirus, respiratory syncytial virus, enterovirus, and human metapneumovirus. MuLBSTA stands for Multilobular infiltration (5 points), Lymphopenia (ALC $<800/ \mu\text{L}$, 4 points), Bacterial coinfection (4 points), Smoking history (current: 3 points, ex-smoker: 2 points, never: 0 points),

hypertension (2 points) and Age (≥ 60 years, 2 points). Using a 12-point cut off value, Guo L et al., reported 78% sensitivity and specificity in identifying 90-day in hospital mortality among viral pneumonia patients. Scores between 0-11 are considered low risk and scores between 12 to 22 are considered high risk. Advantages of this scoring system is that, all data is available at the time of admission and does not require special investigations.⁴⁴

CURB-65

It is a simple predictive tool widely used to predict the 30-day mortality in community acquired pneumonia and 14-day mortality in hospital acquired pneumonia.^{45,46} It helps to determine the inpatient vs outpatient treatment. The scoring system is shown in Table 2. Based on points, 0-1 are considered low risk and points equal to or more than 2 are considered moderate and high risk.⁸

Table 2: CURB-65 scoring system

Feature	Point
Confusion	1
Urea > 7 mmol/L	1
Respiratory rate ≥ 30	1
Systolic blood pressure ≤ 90 mmHg or diastolic blood pressure ≤ 60 mmHg	1
Age over 65 years	1

HNC-LL

Xiao LS et al., developed the HNC-LL model to predict severity of COVID-19. HNC-LL stands for hypertension, neutrophil count, C-reactive protein, lymphocyte count, lactate dehydrogenase. The formula used to determine the HNC-LL score:

HNC-LL score =

$$\begin{aligned} & \mathbf{1.035 \times \text{neutrophil count (1: } \geq 6.3 \times 10^9/\text{L; 0: } < 6.3 \times 10^9/\text{L)}} \\ & \mathbf{- 1.237 \times \text{lymphocyte count (1: } \geq 1.1 \times 10^9/\text{L; 0: } < 1.1 \times 10^9/\text{L)}} \\ & \mathbf{+ 1.419 \times \text{CRP level (1: } \geq 10 \text{ mg/L; 0: } < 10 \text{ mg/L)}} \\ & \mathbf{+ 1.066 \times \text{LDH (1: } > 245 \text{ U/L; 0: } \leq 245 \text{ U/L)}} \\ & \mathbf{+ 0.969 \times \text{hypertension (1: with; 0: without)} - 2.425} \end{aligned}$$

Based on optimum cut off value, -1.508, a score of (≥ -1.508) is considered high risk and score (< -1.508) is considered low risk. Patients with Mild to moderate COVID-19 infection, who are categorized as high risk based on HNC-LL score require active treatment and close monitoring to prevent disease progression. The main strength is the simplicity of application in the clinical setting, whereby it has the advantage of including a small number of parameters that are easily and routinely measured in hospitalized patients with respiratory infections.³

Related studies

Guo L, et al (2019)⁴⁴ examined 528 patients with viral pneumonia to identify any relevant clinical traits that could indicate mortality risk. On admission, information was gathered on demographics, comorbidities, routine laboratory tests, immunological indices, etiology detection methods, radiographic imaging, and treatment. 90-day in-hospital mortality rate was 14.4%. Based on a multivariate logistic regression model, predictive MuLBSTA score was calculated to predict mortality. “It included multilobular infiltrates (OR = 5.20, 95% CI 1.41-12.52, $p = 0.010$; 5 points), lymphocyte $\leq 0.8 \times 10^9/L$ (OR = 4.53, 95% CI 2.55-8.05, $p < 0.001$; 4 points), bacterial coinfection (OR = 3.71, 95% CI 2.11-6.51, $p < 0.001$; 4 points), acute-smoker (OR = 3.19, 95% CI 1.34-6.26, $p = 0.001$; 3 points), quit-smoker (OR = 2.18, 95% CI 0.99-4.82, $p = 0.054$; 2 points), hypertension (OR = 2.39, 95% CI 1.55-4.26, $p = 0.003$; 2 points) and age ≥ 60 years (OR = 2.14, 95% CI 1.04-4.39, $p = 0.038$; 2 points).” The model demonstrated 78% sensitivity, 78% specificity, and greater predictive performance than CURB-65 utilizing TWELVE points as the criterion (AUROC = 0.773 vs. 0.717, $p < 0.001$). The authors concluded that MuLBSTA score can be used to predict mortality among viral pneumonia patients.

Xiao LS, et al (2020)³ conducted a study with the goal of creating a predictive model for COVID-19 severity. 442 participants were included for the analysis out of the total 690 individuals having a proven SARS CoV-2 diagnosis between 1 January and 18 March 2020 who were a part of the study. For the construction and validation of the HNC-LL model, the obtained data was split into a training set and a test set. Multivariate logistic regression analysis was used to obtain the predictive HNC-LL score. HNC-LL was better predicting disease severity with AUC of 0.861 and 0.871

in Honghu training and internal validation cohort, respectively and with an Area Under Curve of 0.826 of Nanchang cohort (p value <0.001, for all). It also outperformed other models such as CURB-65, MuLBSTA and NLR, thus confirming the predictability of disease severity among COVID-19 patients. The authors concluded that this model can be used to identify severe disease and help in treatment decisions.

Laguna-Goya R, et al (2020)⁴⁷ carried out a study with an aim to develop a model that predicts the disease outcome in COVID-19 patients. In Spain, 611 adult patients with COVID-19 were diagnosed between 10 March 2020 and 12 April 2020. 501 patients who were discharged or died by 20 April 2020 were included in the analysis. Results suggested that elevated levels of IL-6, CRP, LDH, ferritin, D-dimer, neutrophil count and NLR were predictive of mortality with an AUC of >0.70. Similarly, decreased levels of albumin, lymphocyte count, monocyte count, SpO₂/FiO₂ were also predictive of mortality. Multivariate logistic regression showed age, SpO₂/FiO₂ ratio, NLR, Lactate Dehydrogenase level, Interleukin-6 level, were high predictors of mortality with AUC of 0.94. The cut off was able to classify patients as survivors and non-survivors with 88% sensitivity and 89% specificity. The authors concluded that mortality risk models are beneficial in risk stratification at the early visit of COVID-19 patient and thereby guides clinical decision making.

Liu Y, et al (2020)⁴⁸ conducted a retrospective study to evaluate the role of NLR in predicting in-hospital mortality among Chinese patients. The relationship between baseline NLR and in-hospital mortality were assessed using univariate and multivariate logistic regression models. Among the 245 COVID-19 patients included, in-hospital mortality was 13.47%. According to the multivariate analysis, for every

unit increase in the NLR, the risk of in-hospital mortality increased by 8% (Odds ratio [OR; 95% CI] = 1.08 [1.01-1.14]; P = 0.0147) in overall population and 10% in males (1.10 [1.02-1.19; P = 0.016). Upon adjustment with confounders, the NLR of patients in the highest tertile had a 15.04 - fold higher risk of death than patients in the lowest tertile, (16.04 [1.14 to 224.95]; P = 0.0395). The authors concluded that NLR can be used as an independent predictor of in-hospital mortality among COVID-19 patients, particularly males.

Pan F, et al (2020)⁴⁹ conducted a case control study to evaluate the possible parameters which could predict the prognosis of hospitalized COVID-19 patients from January 2020 to March 2020. A total of 124 patients [discharge group (n=35) and death event group (n=89)] are analysed in the group. In the bivariate comparison, gender, SpO₂, respiratory rate, diastolic blood pressure, neutrophil, lymphocyte, CRP, PCT, LDH and D-dimer are associated with increased mortality. Subsequent multivariate logistic regression analysis demonstrated “SpO₂≤89%, lymphocyte≤0.64×10⁹/L, CRP>77.35mg/L, PCT>0.20μg/L, and LDH>481U/L were the independent risk factors with the ORs of 2.959, 4.015, 2.852, 3.554, and 3.185, respectively (p<0.04).” Compared to discharge group, there was increased levels of C Reactive Protein, Procalcitonin, Interleukin-6, Neutrophil, LDH, D-dimer, TROPONIN I, BNP, and high CD4+: CD8+ T-lymphocyte and lower lymphocyte count among patients in death events group. The authors concluded that systematic inflammation with cardiac dysfunction may likely result in mortality.

In a retrospective study, **Satici C, et al (2020)**⁸ evaluated the reliability of CURB-65 and the pneumonia severity index (PSI) in determining 30-day mortality in COVID-19 patients, as well as the need to find other risk factors for increased mortality. 681 laboratory confirmed COVID-19 patients from a pandemic hospital in Istanbul, Turkey have been studied. Data including presenting symptoms, vital signs and lab investigation reports were collected. Elevated CRP levels were significantly increased the risk of mortality (Odds ratio [95%CI]: 1.015[1.008-1.021]; $p < 0.001$). Compared to CURB-65, PSI was better in predicting the mortality risk “(AUC: 0.88, 95% CI: 0.85-0.90 vs. AUC: 0.91, 95% CI: 0.88-0.93; $p = 0.01$)”. However, the PSI index's effectiveness in predicting mortality did not increase with the inclusion of CRP to it “(AUC: 0.91, 95% CI: 0.88-0.93 vs AUC: 0.92, 95% CI: 0.89-0.94; $p = 0.29$)”. The authors concluded that although PSI is better than CURB -65 in predicting mortality, addition of another parameter CRP does not improve the 30-day mortality prediction rate.

Ye W, et al (2020)⁵⁰ conducted a retrospective study among 349 hospitalized patients with COVID-19 diagnosis, to assess D-dimer and Neutrophil-Lymphocyte Count Ratio (NLR) as a marker for improvement of COVID-19 for clinical use. Receiver operating characteristics (ROC) and COX regression analysis were used to explore the optimum cut off values and dynamic changes in D-dimer and NLR. 10% of patients are intubated and 14.9% died. D-dimer and Neutrophil to Lymphocyte Ratio was significantly high among deceased patients than survivors ($p < 0.001$) and intubated patients than non-intubated patients ($p < 0.001$). Similarly, comparing deceased patients, and initial D-dimer (Mean difference [95% CI]: -25.23 [- 31.81 to -18.64]; $P < 0.001$) and NLR (-43.73 [59.28 to -31.17], $P < 0.001$) were significantly lower than peak values. The areas under ROC of peak D-dimer “(0.94[95%CI: 0.90–

0.98] vs. 0.80 [95% CI: 0.73–0.87]) and NLR (0.93 [95%CI:0.90–0.96] vs. 0.86 [95%CI:0.82–0.91])” were also higher than initial tests. The cut-off value of initial D-dimer, peak D-dimer, initial NLR and peak NLR was 0.73 mg/L, 3.78 mg/L, 7.13 and 14.31 respectively for survival analysis and 0.73 mg/L, 12.75 mg/L, 7.28 and 27.55, respectively to predict intubation. The authors concluded that D-dimer and NLR can be used as predictive markers to identify disease severity in COVID-19 patients.

Zheng Y, et al (2020)⁵¹ retrospectively compared the differences in the hemogram and dynamic profiles in patients with severe and non-severe COVID-19 to identify the markers for disease severity. A total of 141 confirmed COVID-19 patients were enrolled in the study. According to the study, on the day of admission most patients had normal WBCs (87.9%), neutrophils (85.1%) and platelets (88.7%). Upon onset of symptoms, 82.8% patients with severe disease had lymphopenia which decreased exponentially with disease progression. Based on multivariate Cox analysis, neutrophils Count “(hazard ratio [HR] = 4.441, 95% CI = 1.954-10.090, p = 0.000), lymphocyte count (HR = 0.255, 95% CI = 0.097-0.669, p = 0.006) and platelet count (HR = 0.244, 95% CI = 0.111-0.537, p = 0.000)” were identified as significant risk factors for infection. Authors concluded that these parameters can be used in predictive models to stratify patients based on severity and aid in decision making.

Iijima Y, et al (2021)⁵² conducted a study to assess MuLBSTA score to estimate the risk of mortality in patients with Corona virus infection. 72 participants with positive COVID-19 infection between 1 April 2020 and 13 March 2020 were included. Based on the extent of respiratory failure, patients were categorized as mild, moderate, and severe groups. In their study, of the 46 patients with mild disease at admission, 17

moderate or severe infection later on. MuLBSTA scoring with a cutoff value of 5 points revealed a sensitivity of 100% and a specificity of just 34.5%. Furthermore, 55 patients with mild or moderate disease, 6 had severe disease; with 11 points, MuLBSTA scoring showing 83.3% sensitivity and 71.4% specificity. The authors concluded that MuLBSTA scoring system can be used a predictive tool for COVID-19 severity.

Malik P, et al (2021)⁵³ conducted a systematic review and meta-analysis to evaluate the association between biomarkers and outcomes in hospitalized COVID-19 patients. The analysis comprised a total of 32 observational studies covering the laboratory results and outcomes of 10,491 confirmed COVID-19 patients who were hospitalized patients. According to result, lymphopenia “(pooled-OR: 3.33 (95% CI: 2.51-4.41); $p < 0.00001$), thrombocytopenia (2.36 (1.64-3.40); $p < 0.00001$), elevated D-dimer (3.39 (2.66-4.33); $p < 0.00001$), elevated CRP (4.37 (3.37-5.68); $p < 0.00001$), elevated PCT (6.33 (4.24-9.45); $p < 0.00001$), elevated CK (2.42 (1.35-4.32); $p = 0.003$), elevated AST (2.75 (2.30-3.29); $p < 0.00001$), elevated ALT (1.71 (1.32-2.20); $p < 0.00001$), elevated creatinine (2.84 (1.80-4.46); $p < 0.00001$) and LDH (5.48 (3.89-7.71); $p < 0.00001$)” were independently linked with greater risk of poor outcomes. The authors concluded that these markers can be considered as early biomarkers to detect severity and improve management of COVID-19 patients.

In a retrospective, single center study, **Oliva A, et al (2021)**⁵⁴ evaluated the capacity of C-Reactive Protein (CRP) to predict intra-hospital mortality and ICU admission in patients with COVID-19 infection using CURB-65, extended CURB-65, PSI, and CALL scores. A total of 224 patients with signs of pneumonia due to SARS CoV2 were included. From medical records, demographics, clinical, laboratory and

radiological data were collected and the above indices were calculated. The mortality rate was 11%. Among the indices, AUC was better for PSI (0.890 vs 0.885 vs 0.858 vs 0.743) compared to extended CURB-65, CURB-65 and CALL scores, respectively. Another measure that boosted the accuracy of predicting in-hospital mortality was a drop in serum albumin to CURB-65 (AUC=0.905). Authors concluded that adding albumin levels to the current CURB-65 score can improve the prediction of mortality in patients with SARS-CoV-2 pneumonia.

Bradley J, et al (2022)⁵⁵ conducted a post-hoc analysis of two prospective cohorts to compare and evaluate efficacy of PSI and CURB-65 in predicting in-hospital mortality secondary to COVID-19 community acquired pneumonia (CAP) vs. non-SARS-COVID CAP. The in-hospital mortality rate was 19% and 6.5% among patients with SARS-CoV2 CAP and non-SARS-CoV2 CAP, respectively. The AUC for PSI score was 0.82 (95% CI, 0.78-0.86) and 0.79 (95% CI, 0.77-0.80) and AUC for CURB-65 score was 0.79 (95% CI, 0.75-0.84) and 0.75 (95% CI, 0.73-0.77) for patients with SARS-CoV-2 CAP and non-SARS-CoV-2 CAP, respectively. Among COVID-19 CAP, addition of D-dimer and procalcitonin did not improve the prognostic performance of predictive models. The authors concluded that both PSI and CURB-65 score are beneficial in predicting mortality regardless of cause.

Kurien SS et al. (2022)⁵⁶ in a retrospective cross-sectional” study to evaluate the clinical and laboratory profile and the risk factors associated with mortality in COVID-19. The study included 391 laboratory-confirmed COVID-19 positive inpatients with an average age of 53.2 years. On bivariate analysis, mean values of total leukocyte count (11.9 vs 7.5 $\times 10^9/L$), absolute neutrophil count (10.5 vs 5.3 $\times 10^9/L$), NLR (11.6 vs 3.4), CRP (185 vs 48 mg/L), ferritin (829.4 vs 323.6 ng/ml),

LDH (905.5 vs 485.1U/L), D-dimer at admission (4.01 vs 1.29 µg/ml), PT INR (1.21 vs 0.99), blood urea nitrogen (105.1 vs 33.6 mg/dl), creatinine (3.6 vs 1.1 mg/dl), were significantly higher in non-survivors than in survivors ($p < 0.001$, for all). Similarly, the mean Absolute lymphocyte count (1.3 vs $2.0 \times 10^9/L$; $p < 0.001$), serum albumin (3.0 vs 3.8 g/dl; $p < 0.005$), and A/G ratio (0.9 vs 1.2 ; $p < 0.001$) were lower in non-survivors than in survivor. Based on multivariate analysis ANC, D-dimer at admission, CRP, and BUN were independent predictors of mortality.

Martin J, et al (2022)⁵⁷ compared the prognostic performance of Sequential Organ Failure Assessment (SOFA), Quick SOFA (qSOFA), CURB-65, Respiratory Rate and Oxygenation (ROX) index and Coronavirus Clinical Characterization Consortium (4C) score to predict mortality and ICU admission among 2122 patients admitted to the hospital for acute COVID-19 infection. In their study, frequency of ICU admission and 30-day mortality rate were 10.2% and 14.3%, respectively. 30-day mortality was better predicted by 4C score (AUC 0.82) than SOFA (AUC 0.75), qSOFA (AUC 0.59), CURB-65 (AUC 0.75) and ROX index (AUC 0.68,). On the other hand, compared to 4C score (AUC 0.62), CURB-65 (AUC 0.60), SOFA (AUC 0.74) and qSOFA (AUC 0.59), ROX index was better at predicting ICU admissions (AUC 0.79). The authors concluded that scores having age and/or comorbidities are better at predicting mortality and those that assess hypoxemia are better at predicting ICU admission.

Parthasarathi A, et al (2022)⁵⁸ conducted a systematic review to assess the role of on admission NLR in predicting COVID-19 disease outcome including severity and mortality. A total of 64 studies including 15,683 patients were included in this pooled analysis. The standardized mean difference (SMD) of NLR between severe and non-

severe patients was 3.12 (95% CI: 2.64–3.59) and between survivors and non-survivors was 3.93 (95% CI: 2.35–5.50). The ROC analysis of NLR showed 80.2% (95% CI: 74.0–85.2%) sensitivity and 75.8% (95% CI: 71.3–79.9%) specificity for the prediction of severity and 78.8% (95% CI: 73.5–83.2%) sensitivity and 73.0% (95% CI: 68.4–77.1%) specificity for mortality. These were independent of age, gender, or comorbidities. The authors concluded that in admission NLR is a good biomarker to predict the severity and mortality in COVID-19 patients and NLR of greater than 6.5 has increased odds of mortality.

MATERIALS AND METHODS

Source of Data

Patients diagnosed with COVID-19 and admitted in the Department of General Medicine, Jawaharlal Nehru Medical College, Belagavi

Study design

Observational study

Study period

01 October 2020 to 30 December 2021

Sample size

Purposive sampling was done. The sample size for the study was calculated using the formula as shown below.

$$N = \frac{4PQ}{D^2}$$

Where,

N=Sample size

P = Prevalence of the disease

Q= 100- P

D = Absolute error taken as 10%

By imputing the values, P=50, Q=50 and D=10 in the formula, a sample size of 100 was required.

$$N=4*50*50/10^2=100$$

Selection criteria

Inclusion criteria

- Adult patients at or above 18 years
- All patients with RT-PCR or RAT confirmed COVID-19 diagnosis

Exclusion criteria

- Pregnant and lactating women

Methodology

Patients admitted at KLES Dr.Prabhakar Kore Hospital having a positive diagnosis of COVID-19 based on nasal and pharyngeal swab specimen RT-PCR or RAT were included. Patients' demographics and detailed history of patients including symptoms were recorded. Respiratory parameters including respiratory and oxygen saturation were recorded. Blood was drawn and sent for laboratory investigations for haematological markers, inflammatory markers, coagulation markers and biochemical markers. By using the markers, the following disease severity indexes were calculated

- CURB 65 (confusion, Urea levels $>7\text{mmol/L}$, Respiratory rate ≥ 30 cycles/min, Blood pressure $<90/60\text{mmHg}$ and age >65 years)⁸
- MuLBSTA (Multilobe infiltrate, Absolute Lymphocyte count $<0.8 \times 10^9/\text{L}$, Bacterial infection, Smoking history, Hypertension and Age <60 years)⁹
- Neutrophil to lymphocyte ratio (NLR; normal range: 0.78 to 3.53)¹⁰
- HNC-LL (Hypertension $>140/90\text{mmHg}$, Neutrophil count $>6.3 \times 10^9/\text{L}$, C-Reactive protein $>10\text{mg/L}$, lymphocyte count $<1.1 \times 10^9/\text{L}$ and Lactate Dehydrogenase levels $>245\text{U/L}$)¹¹

- Finally, the disease severity indices were then used to calculate the severity of COVID-19 (mild, moderate and severe) in our study population.

Disease progression was monitored including duration of hospital stay. Patients were categorized as, either improved or expired. Comparison of demographics, respiratory parameters, blood biomarkers and disease outcome were assessed. Similarly, comparison of disease severity based on MuLBSTA, NLR, CURB65 and HNC-LL and disease outcome was compared. The optimum cut off values for HNC-LL which will predict the disease severity and outcome was estimated. Further, the sensitivity and specificity of HNC-LL in predicting the severity of COVID -19 were analysed.

Data collection

The following data were collected using a case history proforma specific to the study.

- Patient demographics including age and gender
- COVID-19 symptoms including breathlessness, cough, fever, myalgia and loss of taste
- Oxygen modality used for management of COVID-19 symptoms
- Respiratory parameters:
 - Respiratory rate
 - SpO₂
- Hematological parameters
 - Hemoglobin
 - Total leucocyte count (TLC)
 - Neutrophil %

- Absolute neutrophil count (ANC)
- Lymphocyte %
- Absolute lymphocyte count (ALC)
- Platelets
- Inflammatory markers
 - Serum Ferritin
 - Lactate dehydrogenase (LDH)
 - hs-CRP
 - IL-6
- Coagulation markers
 - Prothrombin time
 - International normalized ratio
 - APTT
 - D-dimer
- Biochemical markers
 - Bilirubin
 - SGOT
 - SGPT
 - AG Ratio
 - Urea
 - Creatinine
 - Serum Procalcitonin
- Outcome of disease: number of hospital days, improvement in symptoms or death

Ethical considerations

Institutional ethical clearance was obtained prior to initiation of the study. The details of the study were explained to the patients and an informed consent was obtained from all patients

Data handling

The collected data were entered in Microsoft excel and the related records were stored safely with no access to other study personnel.

Statistical analysis

Data was analyzed using statistical software R version 4.1.0 and Microsoft Excel. Categorical variables were summarized as frequency and percentages. Continuous variables were presented as Mean and standard deviation or median (minimum, maximum) values. Chi-square test was used to check the association of outcome among categorical variables. For continuous variables, two sample t test/ Welch's t test is used to compare means of variables with outcome. Mann Whitney U test is used to compare the distributions of variables with outcome and severity of disease. Spearman's Correlation test is used to check the correlation of different parameters. P-value less than or equal to 0.05 indicates statistical significance.

RESULTS

A total of 142 patients with COVID-19 infection were included in our study. The mean age and standard deviation (SD) of the study patients was 55.67 ± 15.63 years (Minimum age -25 years and maximum age-91 years) and the median age of the study patients was 55 years. Descriptive statistics of age are described in table 3 and a group wise distribution according to the age in Table 4.

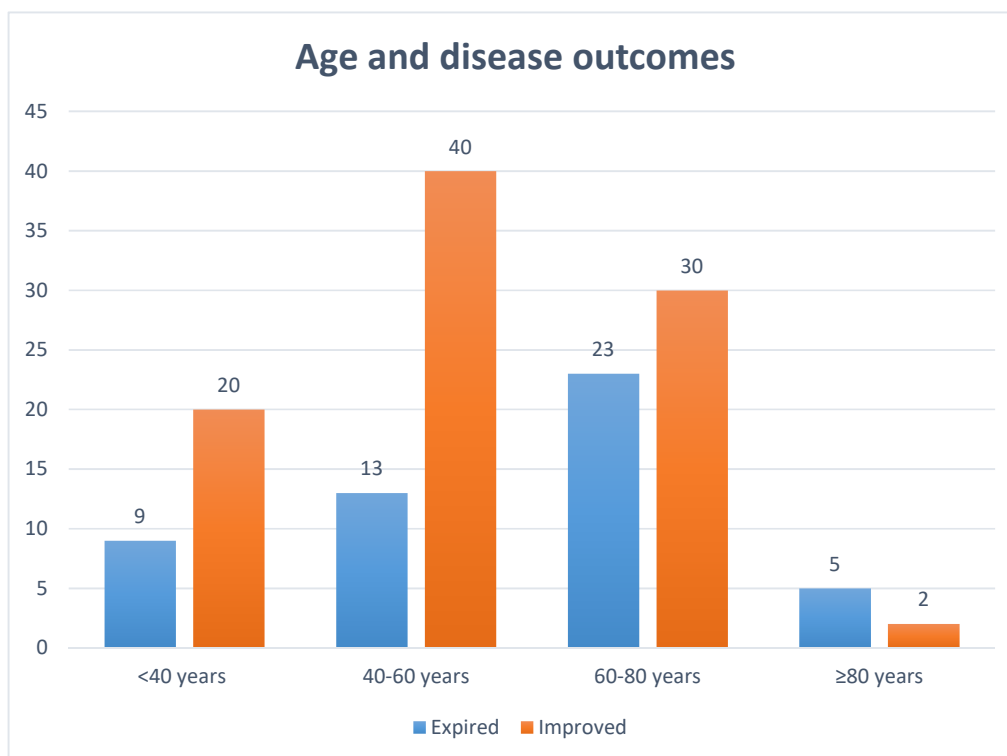
Table 3: Descriptive statistics of age in the study population

Variable	N	Mean	Standard deviation	Median	Minimum	Maximum
Age (years)	142	55.67	15.63	55	25	91

Majority of patients (n=53, 37.32%) belonged to the age group of 40-60 years and 60-80 years followed by, <40 years (n=29, 20.42%) and ≥ 80 years (n=7, 4.93%). Chi-square tests for the outcomes (expired vs improved) was statistically significant. (**p=0.0386**)

Table 4: Group wise distribution of age based on the outcomes

Factors	Groups	Total	Outcome		p-value
			Expired	Improved	
Age (years)	<40	29 (20.42%)	9 (18%)	20 (21.74%)	0.0386
	40-60	53 (37.32%)	13 (26%)	40 (43.48%)	
	60-80	53 (37.32%)	23 (46%)	30 (32.61%)	
	≥80	7 (4.93%)	5 (10%)	2 (2.17%)	

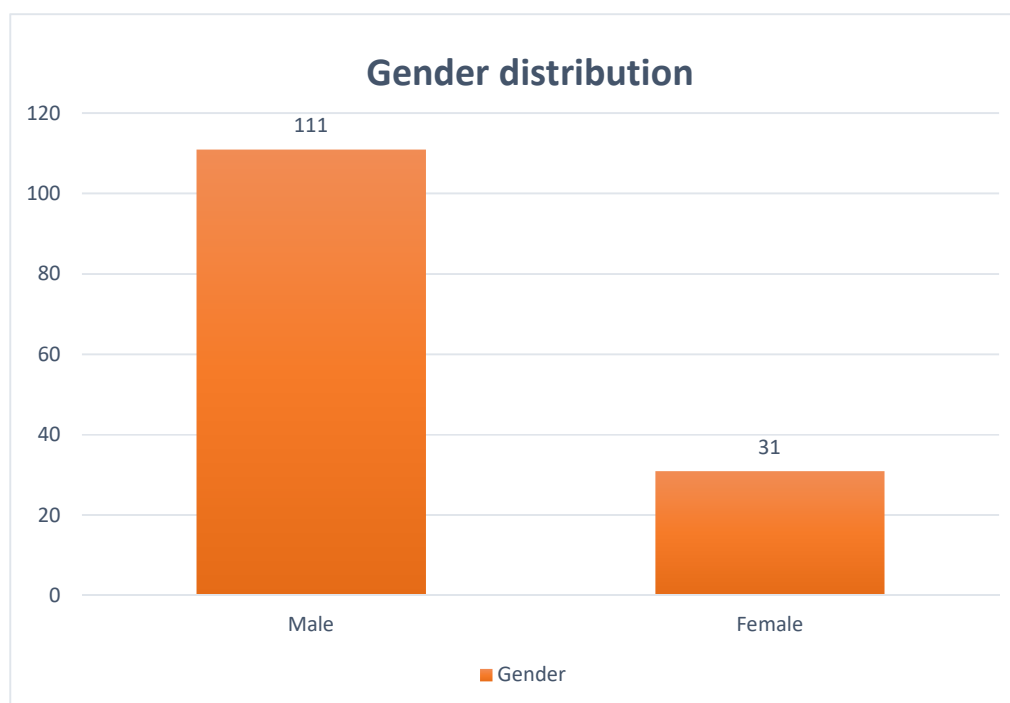


Graph 4: Frequency distribution of age in the study population based on the outcomes

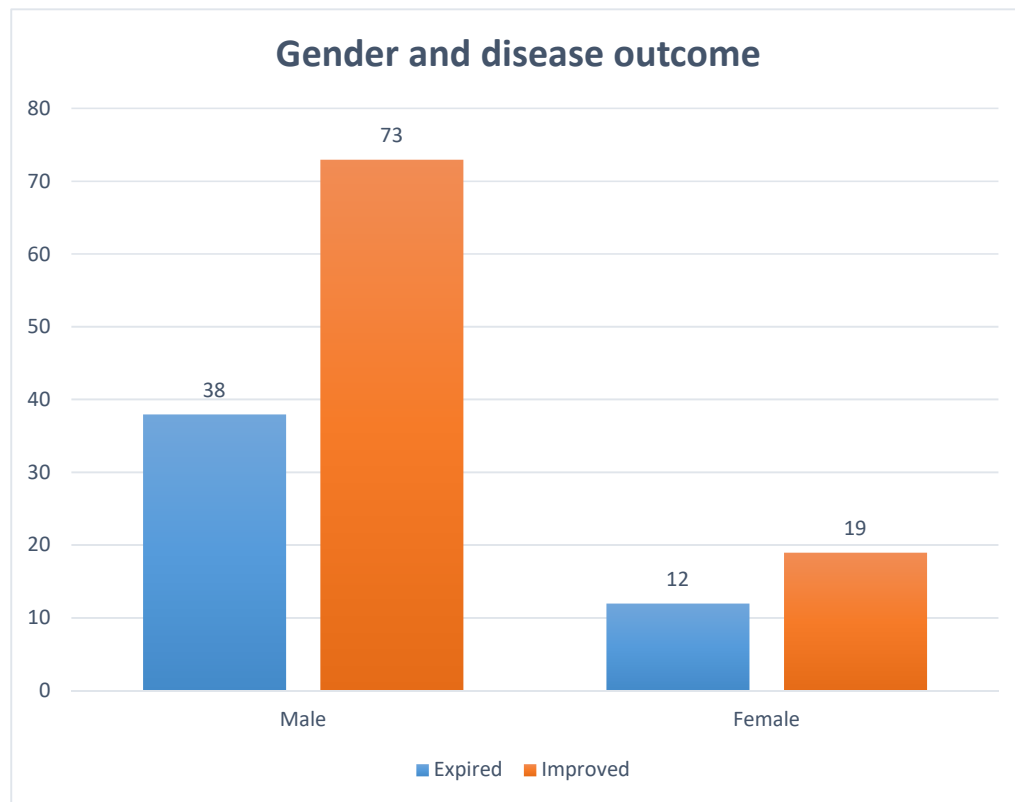
Table 5: Gender distribution of study population

Variable		Frequency N=142	Outcomes		P value
			Expired	Improved	
Gender	Male	111 (78.17%)	38 (76%)	73 (79.35%)	0.6375
	Female	31 (21.83%)	12 (24%)	19 (20.65%)	
Total		142	50	92	

In our study population, majority were males (n=111, 78.17%), followed by females (n=31, 21.83%). Male to female ratio was 3.6:1. Gender distribution is summarized in Table 5 and graph 5 &6.



Graph 5: Frequency distribution of gender in the study population

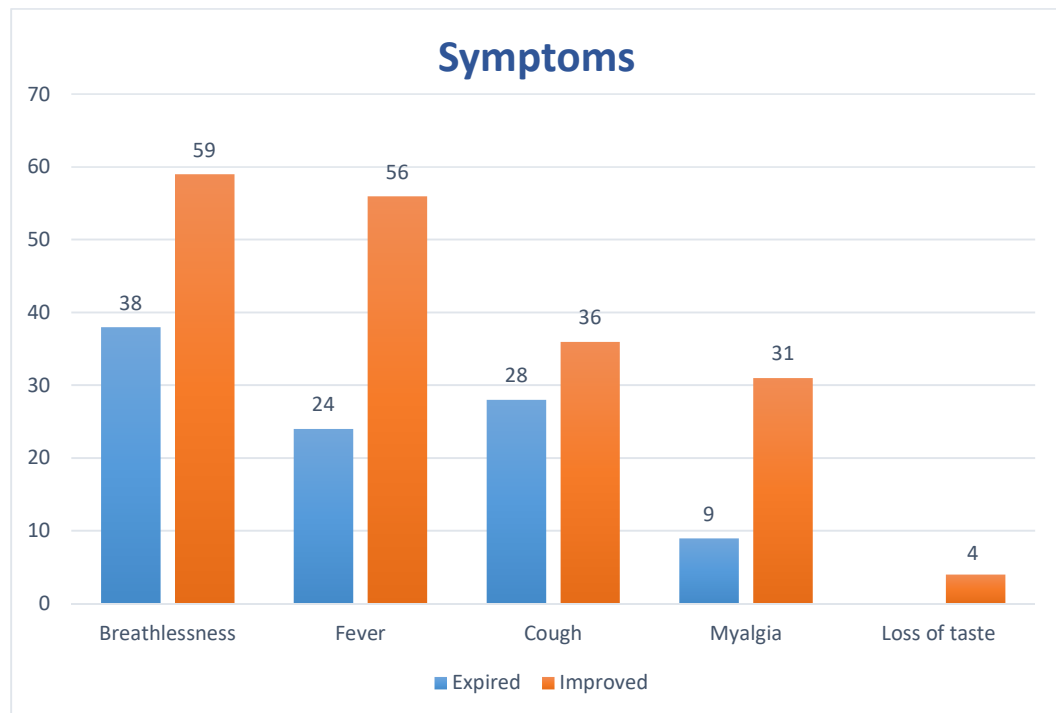


Graph 6: Comparison of disease outcome among gender

Table 6: Distribution of patients based on symptoms

Variable	Groups	Frequency (%) N=142	Outcome		P value
			Expired	Improved	
Symptoms	Breathlessness	97 (68.31%)	38 (76%)	59 (64.13%)	0.1672
	Fever	80 (56.34%)	24 (48%)	56 (60.87%)	0.1423
	Cough	64 (45.07%)	28 (56%)	36 (39.13%)	0.0423
	Myalgia	40 (28.17%)	9 (18%)	31 (33.7%)	0.038
	Loss of taste	4 (2.82%)	0	4 (4.35%)	0.2635
Total		142			

Table 6 and Graph 7 summarizes symptoms distribution among the study population. The most common reported symptom was breathlessness (n=97, 68.31%) followed by fever (n=80, 56.34%), cough (n=64, 45.07%), myalgia (n=40, 28.17%) and loss of taste (n=4, 2.82%). Cough and myalgia symptoms were statistically significant in the improved group ($p=0.0423$ and $p=0.038$ respectively).

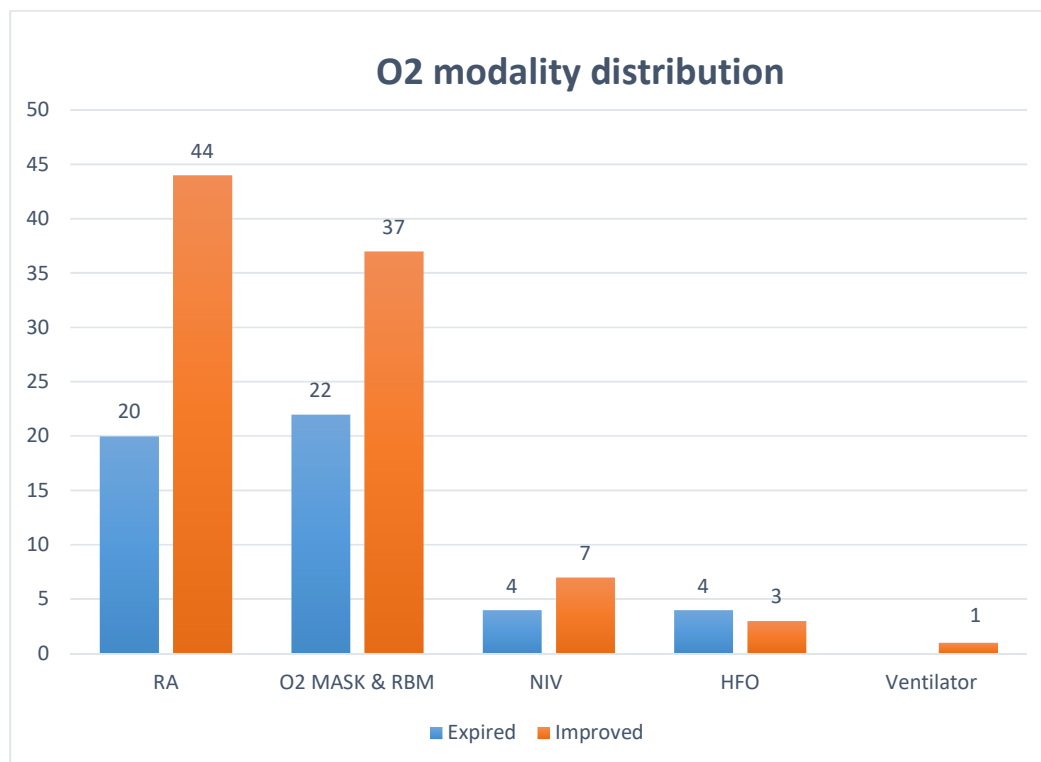


Graph 7: Bar diagram showing symptoms distribution among study population

Table 7: Distribution of patients based on oxygen modality used

Variable	Groups	Frequency N=142	Outcome		P value
			Expired	Improved	
O ₂ modality	RA	64 (45.07%)	20 (40%)	44 (47.83%)	0.2191
	O ₂ MASK	59 (41.55%)	22 (44%)	37 (40.21)	
	NIV	11 (7.75%)	4 (8%)	7 (7.61%)	
	HFO	7 (4.93%)	4 (8%)	3 (3.26%)	
	Ventilator	1 (0.7%)	0	1 (1.09%)	
Total		142	50	92	

Table 7 and graph 8 summarizes the patient distribution based on oxygen modality used by patients during the study period. In our study, majority of the patients were on room air (n=64, 45.07%), (n= 59, 41.6%) were on oxygen mask. Non-invasive ventilation (NIV), high flow oxygen (HFO), and ventilator were needed by 11 (7.75%), 7 (4.93%) and 1(0.7%) patient, respectively. The oxygen modality used was not statistically significant between the expired and improved study participants (p=0.2191).



Graph 8: Bar diagram showing distribution of patients based on oxygen modality usage

Table 8: Descriptive statistics of hospital stay in the overall study population

Variable	N	Mean	Standard deviation	Median	Minimum	Maximum
Hospital Stay (days)	142	9.3	6.85	8	0	41

In our study, the hospital stays due to COVID-19 ranges from 0-41 days with a mean and standard deviation of 9.3 ± 6.85 days and median of 8 days (Table 8).

Table 9: Comparison of hospital stay based on disease outcome

Variables	Sub-Category	Outcome		p-value
		Expired	Improved	
Hospital Stay (days)	Mean \pm SD	6.96 \pm 4.9	10.58 \pm 7.43	0.0024^{t*}
	Median (Min, Max)	6 (0,20)	9 (0,41)	

t-Two sample *t* test, * indicates statistical significance.

In our study, the mean duration of hospital stay was significantly longer in patients who had an improvement in the disease compared to patients who succumbed (10.58 \pm 7.43 days Vs 6.96 \pm 4.9 days; **p=0.0024**. Table 9, Graph 9.

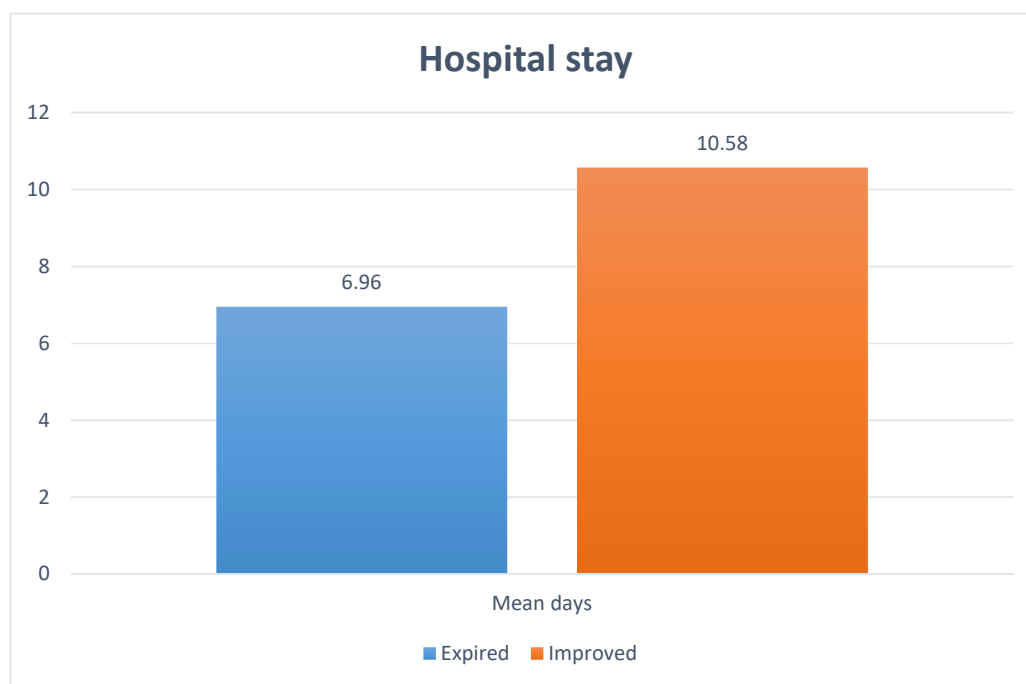
**Graph 9: Distribution of mean hospital stay based on disease outcome**

Table 10: Descriptive statistics of the RR, SpO2 among study population

Variables	Sub-Category	Outcome		p-value
		Expired	Improved	
RR	Mean \pm SD	29.35 \pm 9.64	31.5 \pm 8.15	0.3365*
SpO2	Median (IQR)	85.5 (92.04)	90 (94.02)	0.7832#

*- Independent sample t-test; #- Mann Whitney U test

Table 10 and graph 10 summarizes the descriptive statistics of respiratory parameters among COVID-19 patients. The Mean respiratory rate (RR) was 30.99 ± 8.52 cycles/min and median (range) RR was 29 (17-60) cycles/min. The mean and standard deviation of RR in expired group and the improved group were 29.35 ± 9.64 and 31.5 ± 8.15 respectively ($p=0.3365$). The mean \pm SD and median (range) SpO2 were 86.35 ± 11.68 and 90 (40-100), respectively ($p=0.7832$).

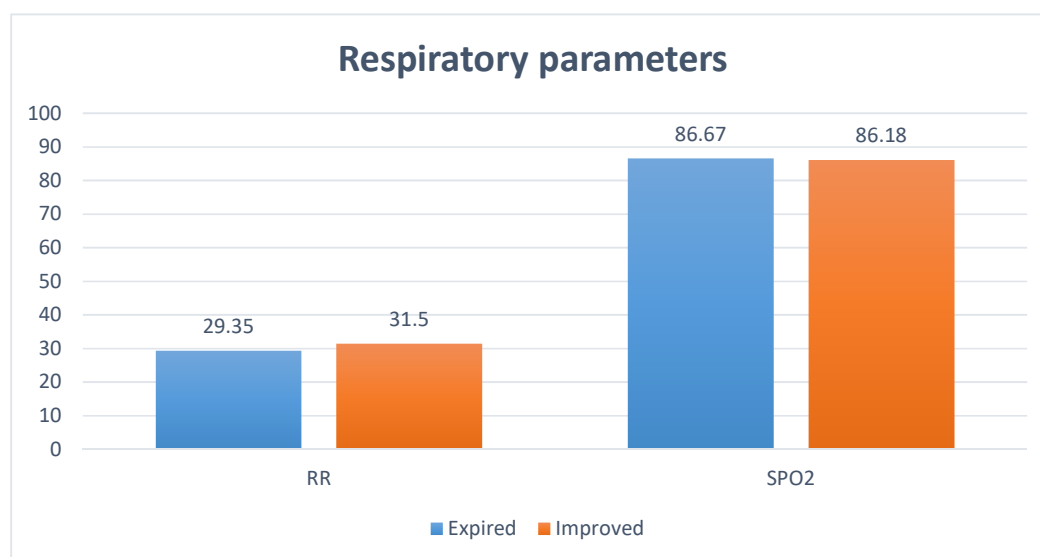
**Graph 10: Comparison of mean RR and Mean SpO2 among expired and improved patients**

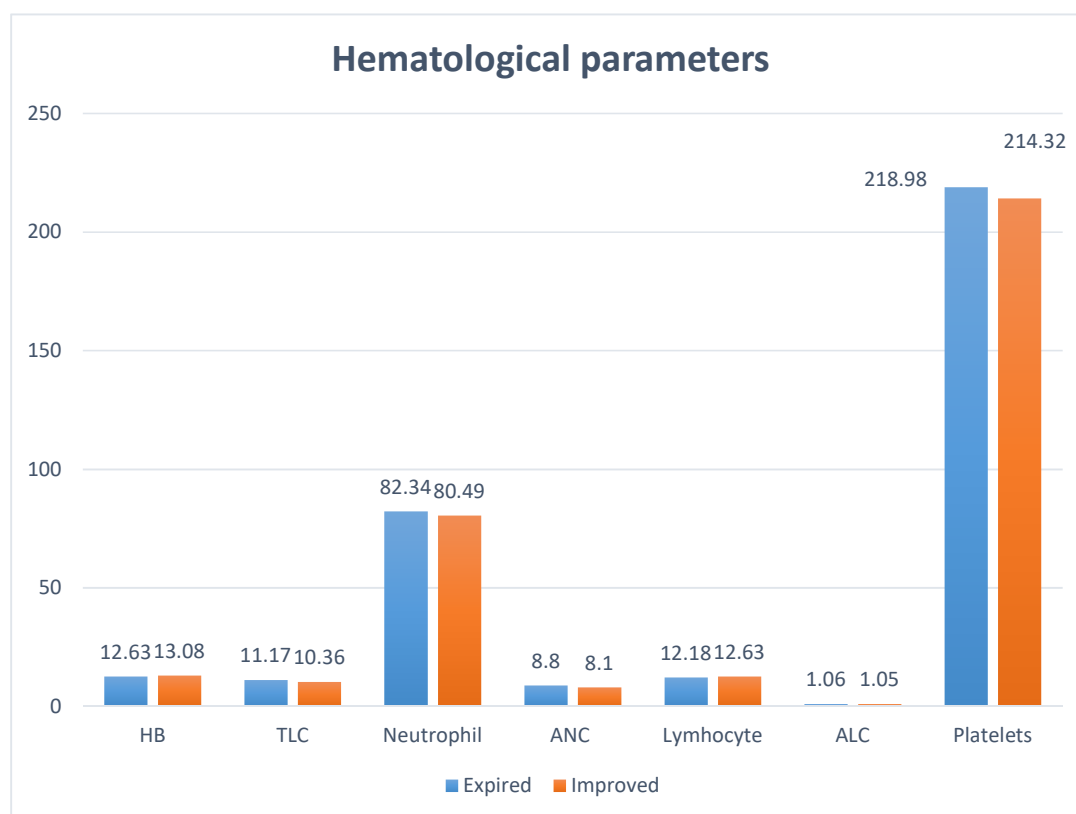
Table 11: Descriptive statistics of the hematological parameters among the study population

Variables	Sub-Category	Outcome		p-value
		Expired	Improved	
Hemoglobin	Mean ± SD	12.63 ± 1.93	13.08 ± 1.88	0.1675*
TLC	Mean ± SD	11.17 ± 6.39	10.36 ± 4.9	0.3962*
Neutrophil%	Mean ± SD	82.34 ± 11.81	80.49 ± 9.97	0.2356*
ANC	Median (IQR)	8.8 (9.2)	8.1 (11.4)	0.1643#
Lymphocyte%	Mean ± SD	12.18 ± 9.67	12.63 ± 8.52	0.7563*
ALC	Mean ± SD	1.06 ± 0.76	1.05 ± 0.58	0.9325*
Platelets(thousands)	Mean ± SD	218.98 ± 91.77	214.32 ± 85.54	0.6758*

***-Independent sample t-test; #-Mann Whitney U test**

Descriptive statistics of the hematological parameters are summarized in Table 11 and graph 11. The mean ± SD and median (range) Hemoglobin levels were 12.92 ± 1.9 and 13.2 (8.4-18.2) g/dL, respectively. Mean and SD of expired and improved groups were 12.63 ± 1.93 and 13.08 ± 1.88 respectively (p=0.1675). The mean ± SD and median (range) Total leucocyte count was 10.65 ± 5.47 and 10.05 (2-33.8) cells/mm³, respectively. The mean and SD of expired and improved groups were 11.17 ± 6.39 and 10.36 ± 4.9 respectively (p=0.3962). The mean ± SD and median (range) neutrophil count was 81.14 ± 10.65% and 83% (41-97), respectively. The mean and SD of expired and improved groups were 82.34 ± 11.81 and 80.49 ± 9.97 (p= 0.2356). The mean lymphocyte count was 12.47 ± 8.91% and 10% (1- 49), respectively. The mean and SD of expired and improved groups were 12.18 ± 9.67

and 12.63 ± 8.52 respectively ($p=0.7563$). The mean \pm SD Absolute neutrophil count (ANC) and absolute lymphocyte count (ALC) were 9.15 ± 5.3 and 1.06 ± 0.65 , respectively. The median (IQR) of ANC of expired and improved groups were 8.8 (9.2) and 8.1 (11.4) respectively ($p= 0.1643$). The mean and SD of ALC of expired and improved groups were 1.06 ± 0.76 and 1.05 ± 0.58 ($p=0.9325$) respectively. The mean \pm SD and median (range) platelet count was 215.96 ± 87.49 and 204.5 (1.22-481), respectively. The mean and SD of expired and improved groups were 218.98 ± 91.77 and 214.32 ± 85.54 ($p=0.6758$) respectively.



Graph 11: Comparison of mean hematological parameters among expired and improved patients

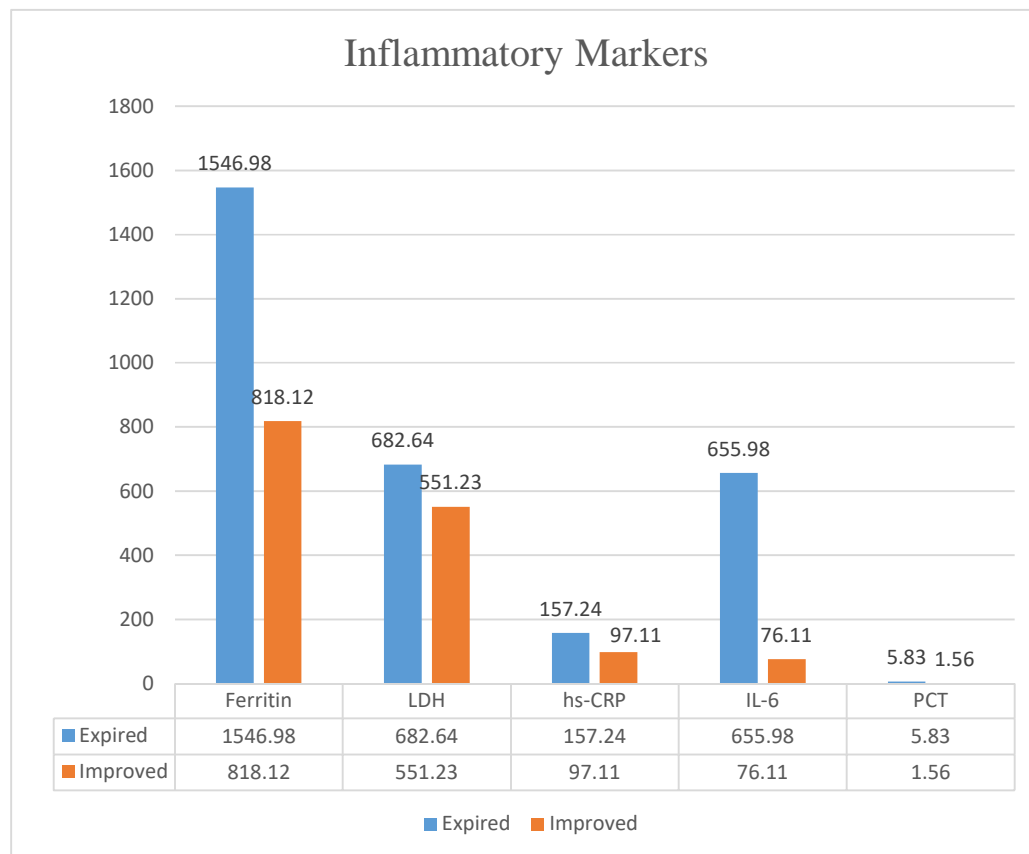
Table 12: Descriptive statistics of the inflammatory markers among the study population

Variables	Sub-Category	Outcome		p-value
		Expired	Improved	
Ferritin	Mean \pm SD	1546.98 \pm 2736.8	818.12 \pm 777.42	0.1134*
LDH	Mean \pm SD	682.64 \pm 370.52	551.23 \pm 395.79	0.0043 *
hs-CRP	Mean \pm SD	157.24 \pm 141.61	97.11 \pm 75.99	0.0342 *
IL-6	Mean \pm SD	655.98 \pm 1545.93	76.11 \pm 105.67	0.0058 *
PCT	Mean \pm SD	5.83 \pm 16.06	1.56 \pm 6.6	0.027 *

*-Independent sample t-test; #-Mann Whitney U test

Descriptive statistics of the inflammatory markers are summarized in Table 12 and graph 12. The mean \pm SD and median (range) of ferritin were 1082.2 \pm 1785.04 ng/mL and 667.5 ng/mL (10.7- 14954), respectively. The mean and SD of expired and improved groups were 1546.98 \pm 2736.8 and 818.12 \pm 777.42 (p=0.1134) respectively. The mean \pm SD and median (range) of lactate dehydrogenase was 596.31 \pm 390.98 U/L and 518 U/L (168-3254), respectively. The mean and SD of expired and improved groups were 682.64 \pm 370.52 and 551.23 \pm 395.79 (p=0.0043). The mean \pm SD and median (range) hs-CRP were 119.05 \pm 108.26 mg/L and 110.2 mg/L (0.4-869.3), respectively. The mean and SD of expired and improved groups were 157.24 \pm 141.61 and 97.11 \pm 75.99 (p=0.0342). The mean \pm SD and median (range) IL-6 levels were 295.9 \pm 990.19 and 47.75 (1.5-6744), respectively in our study population. The mean and SD of expired and improved groups were 655.98 \pm 1545.93 and 76.11 \pm 105.67 (p=0.0058) respectively. The mean \pm SD and median

(range) of Serum PCT were 3.37 ± 13.01 and 0.17 (0-100), respectively The Sr. PCT of mean and SD of `expired and improved groups were 5.83 ± 16.06 and 1.56 ± 6.6 ($p=0.027$) respectively.

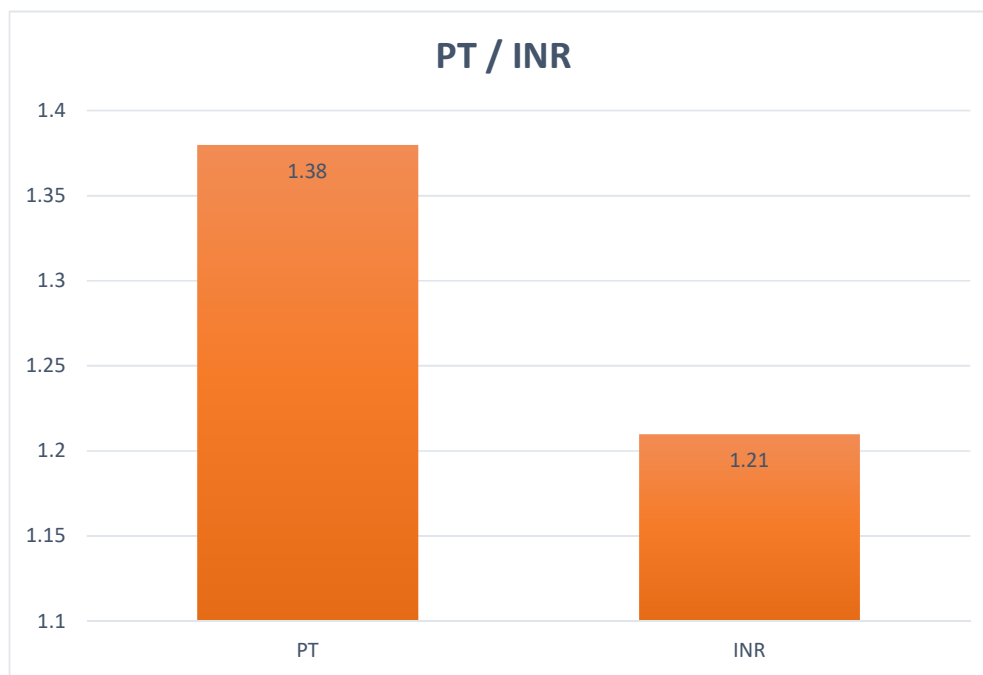


Graph 12: Comparison of mean inflammatory markers among expired and improved patients

Table 13: Descriptive statistics of the coagulation markers among the study population

Variable	N	Mean	SD	Median	Minimum	Maximum
PT	78	1.38	1.49	1.16	0.94	4.2
INR	78	1.21	0.23	1.16	0.94	2.59

Descriptive statistics of the coagulation markers are summarized in Table 13 and graph 13. The mean \pm SD and median (range) of prothrombin time were 1.38 ± 1.49 seconds and 1.16 (0.94-14.2), respectively. The mean \pm SD and median (range) of INR were 1.21 ± 0.23 and 1.16 (0.94-2.59), respectively.



Graph 13: Comparison of PT ratio and INR among the study participants

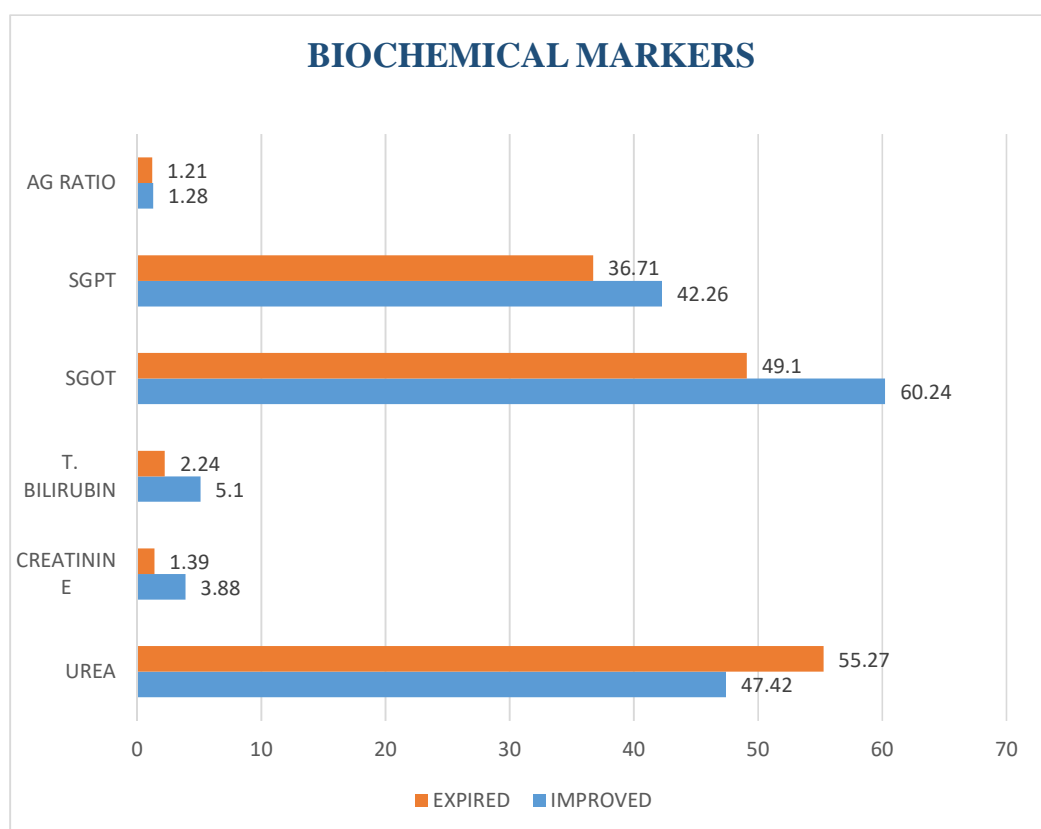
Table 14: Descriptive statistics of the biochemical markers among the study population

Variables	Sub-Category	Outcome		p-value
		Expired	Improved	
Bilirubin (n=137)	Mean \pm SD	2.24 \pm 11.62	5.1 \pm 35.47	0.5782*
SGOT (n=138)	Mean \pm SD	49.1 \pm 32.36	60.24 \pm 113.84	0.5153*
SGPT (n=137)	Mean \pm SD	36.71 \pm 25.33	42.26 \pm 67.17	0.6217*
AG ratio (n=133)	Mean \pm SD	1.21 \pm 0.31	1.28 \pm 0.31	0.2133*
Urea	Mean \pm SD	55.27 \pm 36.14	47.42 \pm 30.4	0.1642*
Creatinine	Mean \pm SD	1.39 \pm 1.24	3.88 \pm 15.01	0.2341*

***-Independent sample t-test**

Descriptive statistics of the biochemical markers are summarized in Table 14 and graph 14. The mean \pm SD and median (range) of bilirubin were 4.09 \pm 29.37 and 0.48 (0.13- 329), respectively. The mean and SD of expired and improved groups were 2.24 \pm 11.62 and 5.1 \pm 35.47 (p=0.5782) respectively. The mean \pm SD and median (range) of SGOT were 56.36 \pm 93.84 and 37 (1.3-767), respectively and of SGPT were 40.31 \pm 56.11 and 30 (10-630), respectively. The mean and SD of SGOT of expired and improved groups were 49.1 \pm 32.36 and 60.24 \pm 113.84 (p=0.5153) respectively. The mean and SD of SGPT of expired and improved groups were 36.71 \pm 25.33 and 42.26 \pm 67.17 (p=0.6217) respectively. The mean \pm SD and median

(range) of AG ratio were 1.26 ± 0.31 and 1.2 (0.7-2.3), respectively. The mean and SD of expired and improved groups were 1.21 ± 0.31 and 1.28 ± 0.31 ($p=0.2133$) respectively. The mean \pm SD and median (range) of Urea were 50.19 ± 32.63 and 41 (8-190), respectively; of creatinine were 3 ± 12.14 and 0.9 (0.15-98), respectively. The mean and SD of urea in expired and improved groups were 55.27 ± 36.14 and 47.42 ± 30.4 ($p=0.1642$) respectively. The mean and SD of creatinine in expired and improved groups were 1.39 ± 1.24 and 3.88 ± 15.01 ($p=0.2341$) respectively.

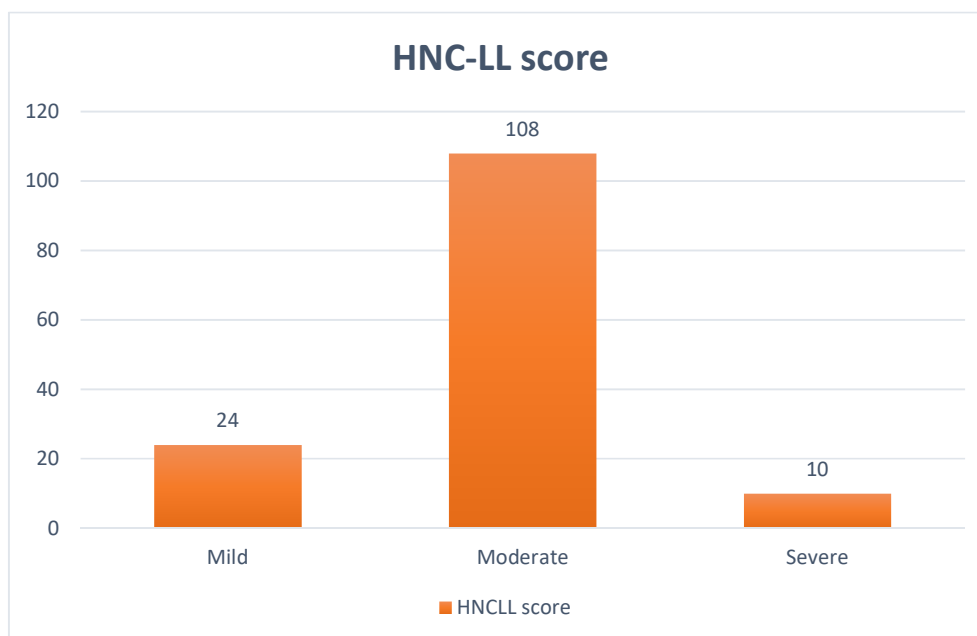


Graph 14: Comparison of mean biochemical markers among expired and improved patients

Table 15: Severity distribution based on HNC-LL scores

Variable		Frequency N=142	Percentage %
HNC-LL score	Mild	24	16.9
	Moderate	108	76.06
	Severe	10	7.04
Total		142	100

Based on HNC-LL scores, 24 (16.9%) patients were categorized as mild disease, 108 (76.06%) were categorized as moderate disease and 10 (7.04%) patients were categorised as severe COVID-19 (Table 15 &16 and Graph 15 & 16).

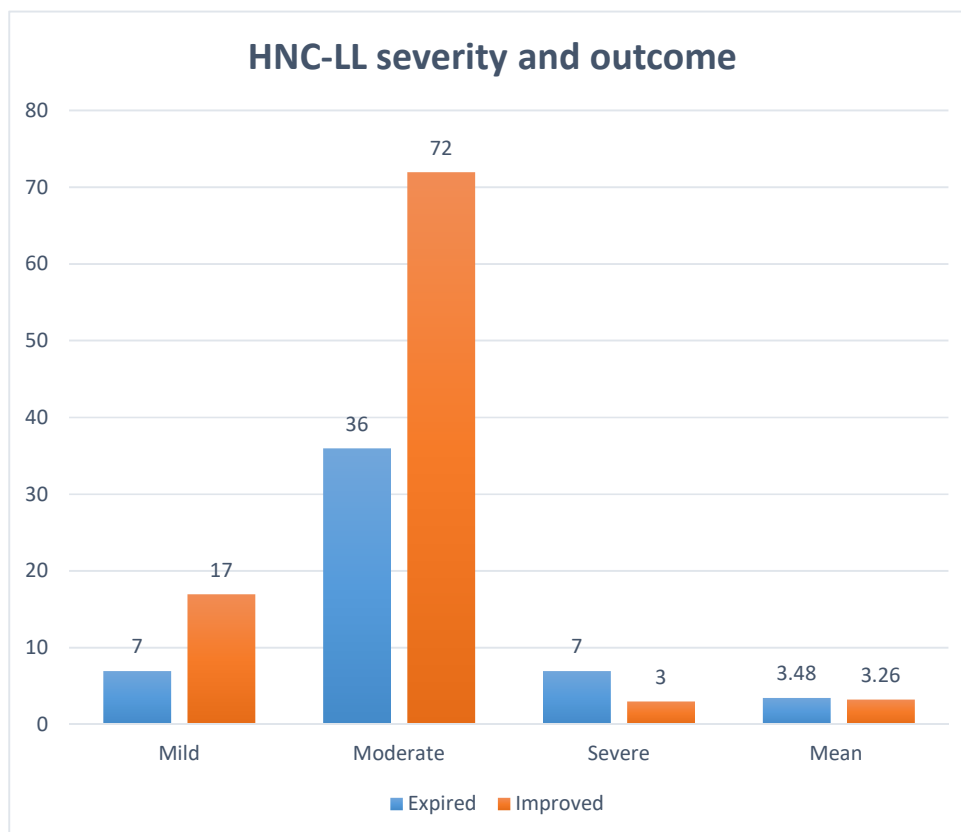


Graph 15: COVID-19 severity based on HNC-LL

Table 16: Comparison of HNC-LL score between expired and improved patients

Variables	Sub-Category	Outcome		p-value
		Expired	Improved	
HNC-LL score	Mild	7 (14%)	17 (18.48%)	0.0635 ^{MC}
	Moderate	36 (72%)	72 (78.26%)	
	Severe	7 (14%)	3 (3.26%)	
	Mean ± SD	3.48 ± 1.05	3.26 ± 0.97	0.221 ^{MW}
Median (Min, Max)	4 (0,5)	3 (1,5)		

MC – Chi square test with Monte Carlo simulation, MW – Mann Whitney U test

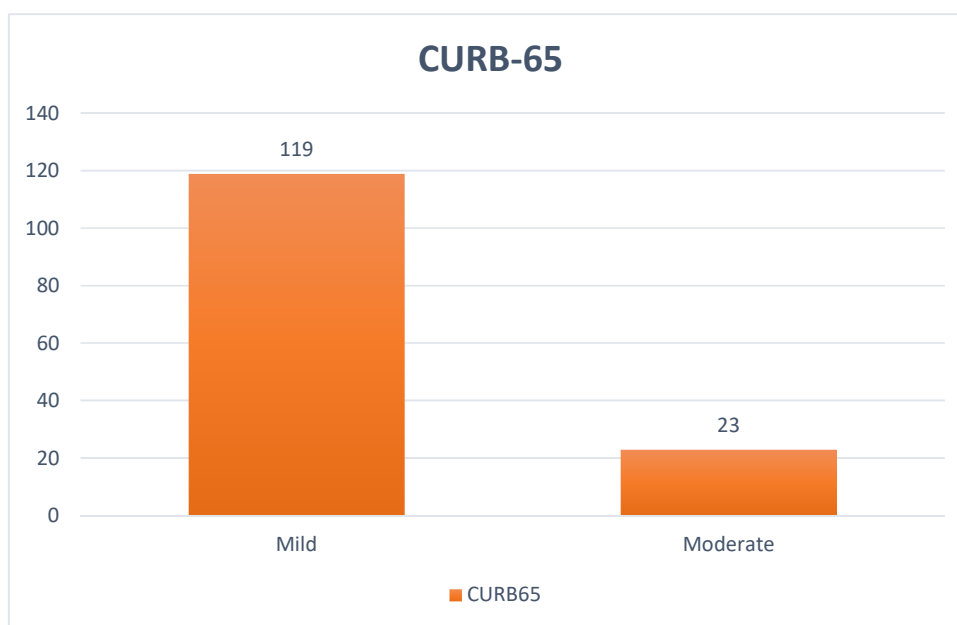


Graph 16: comparison of HNC-LL score between expired and improved patients

Table 17: Severity distribution based on CURB-65 scores

Variable		Frequency N=142	Percentage %
CURB-65	Mild	119	83.8
	Moderate	23	16.2
	Severe	0	0
Total		142	100

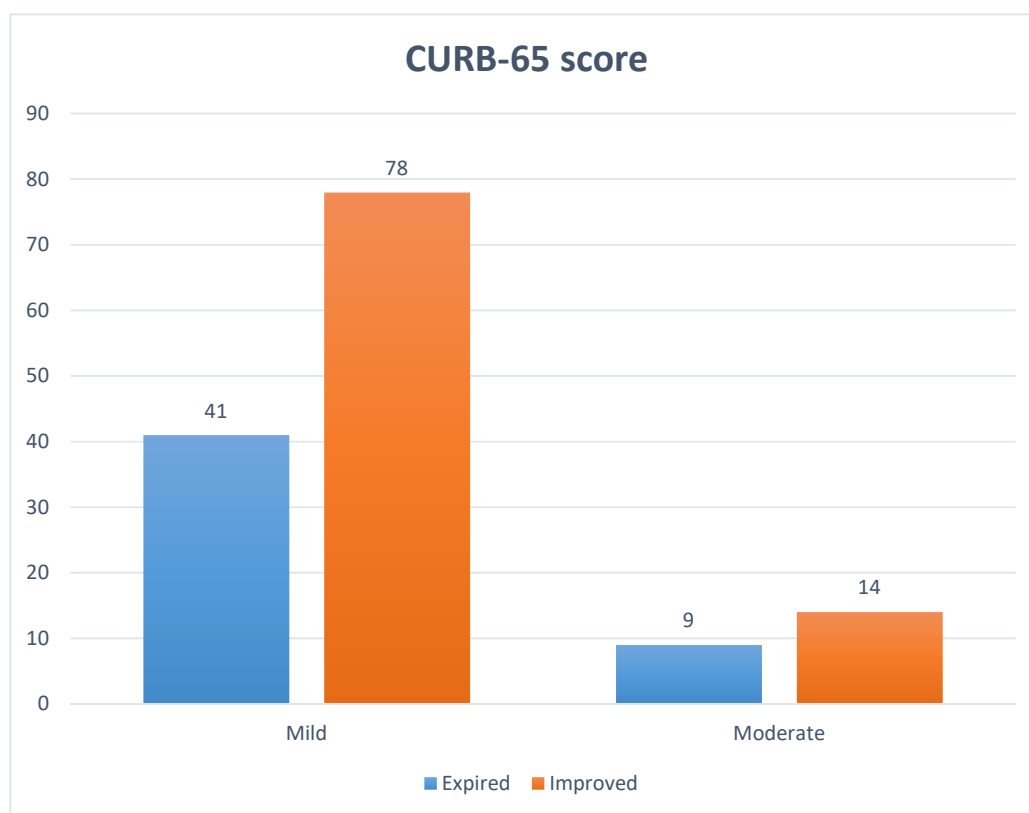
Based on CURB65 indicator, 119 (83.8%) patients were categorised as mild and 23 (16.2%) patients were categorised as severe COVID-19 (Table 17 &18 and Graph 17 & 18).



Graph 17: Severity distribution among CURB-65 Score

Table 18: comparison of CURB-65 score between expired and improved patients

Variables	Sub-Category	Outcome		p-value
		Expired	Improved	
CURB65	Mild	41 (82%)	78 (84.78%)	0.6673 ^C
	Moderate	9 (18%)	14 (15.22%)	
	Mean ± SD	1.7 ± 0.91	1.72 ± 0.82	0.8766 ^{MW}
	Median (Min, Max)	2 (0,4)	2 (0,4)	

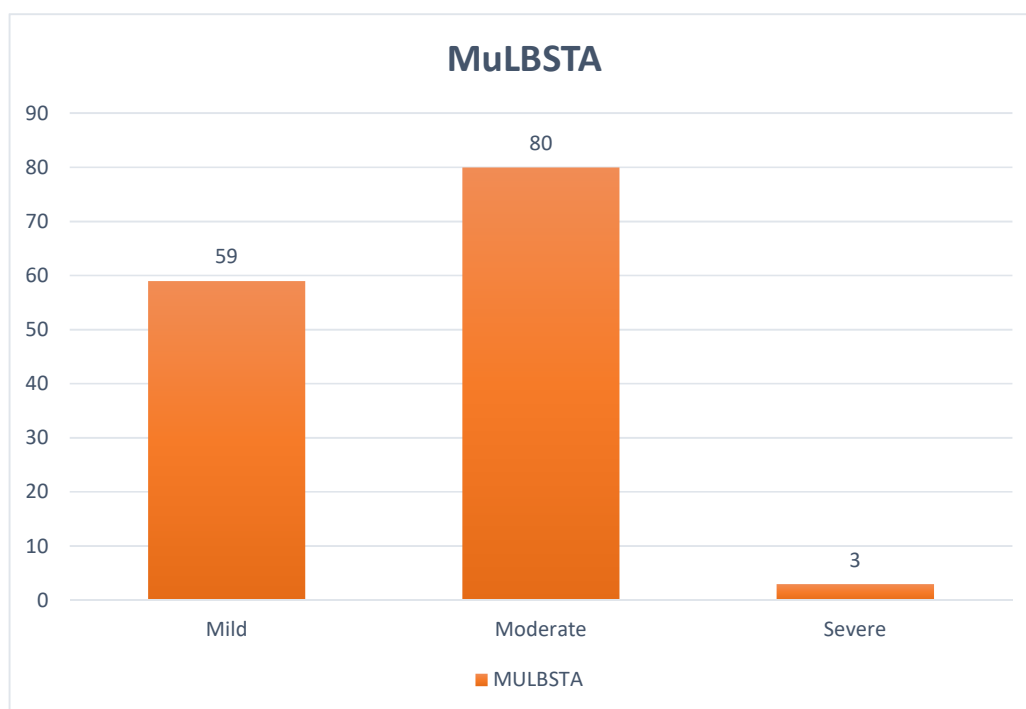


Graph 18: Comparison of CURB-65 score between expired and improved patients

Table 19: Severity distribution based on MuLBSTA

Variable		Frequency N=142	Percentage %
MuLBSTA	Mild	59	41.55
	Moderate	80	56.34
	Severe	3	2.11
Total		142	100

Based on MuLBSTA, 59 (41.55%) patients were categorised as mild disease, 80 (56.34%) were categorised as moderate disease and 3 (2.11%) patients were categorised as severe COVID-19 (Table 19 & 20 and Graph 19 & 20).

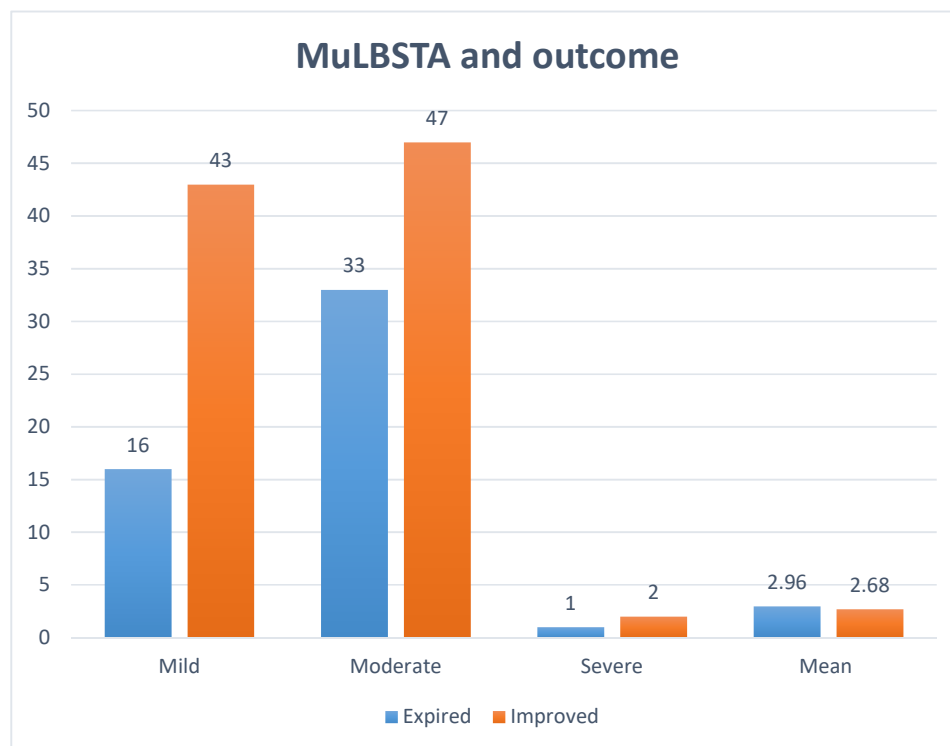


Graph 19: COVID-19 severity based on MuLBSTA

Table 20: comparison of MuLBSTA score between expired and improved patients

Variables	Sub-Category	Outcome		p-value
		Expired	Improved	
MuLBSTA	Mild	16 (32%)	43 (46.74%)	0.2304 ^{MC}
	Moderate	33 (66%)	47 (51.09%)	
	Severe	1 (2%)	2 (2.17%)	
	Mean ± SD	2.96 ± 0.99	2.68 ± 0.89	0.0808 ^{MW}
Median (Min, Max)	3 (1,6)	3 (1,5)		

MC – Chi square test with Monte Carlo simulation, MW – Mann Whitney U test



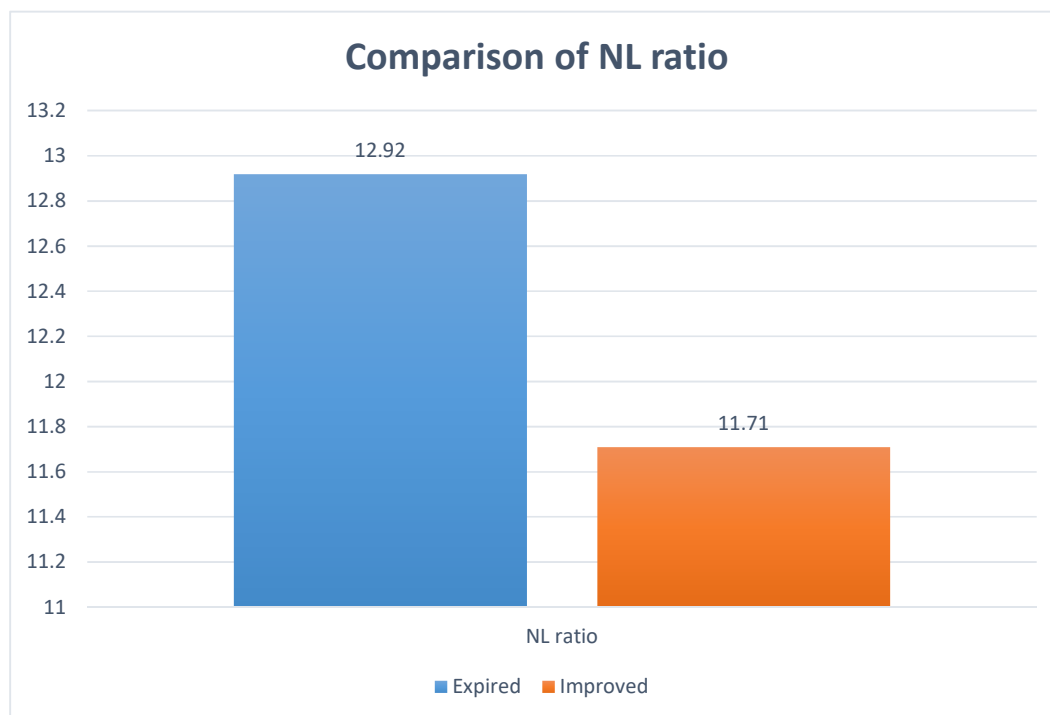
Graph 20: comparison of MuLBSTA score between expired and improved patients

Table 21: comparison of NL ratio between expired and improved patients

Variables	Sub-Category	Outcome		p-value
		Expired	Improved	
NL ratio	Mean ± SD	12.92 ± 13.29	11.71 ± 10.84	0.4876 ^{MW}
	Median (Min, Max)	9.67 (0,79.33)	8.58 (0,54.25)	

MW – Mann Whitney U test

No Significant difference in the Mean ± SD NL ratio between expired (12.92 ± 13.29) and improved (11.71 ± 10.84) patients was observed (p=0.486; Table 21 and Graph 21).

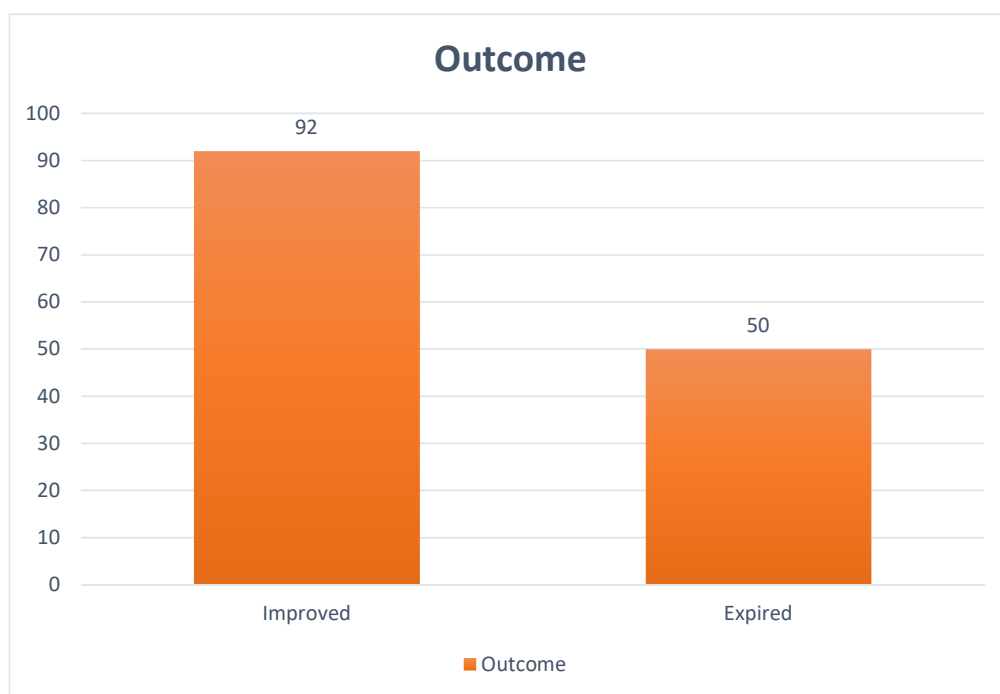


Graph 21: comparison of NL ratio between expired and improved patients

Table 22: COVID-19 disease outcome in the study population

Variable		Frequency N=142	Percentage %
Outcome	Improved	92	64.79
	Expired	50	35.21
Total		142	100

In our study, 92(64.79%) of the 142 patients improved from the disease while 50 (35.21%) patients succumbed. Covid-19 disease outcome is summarized in table 22 and graph 22.



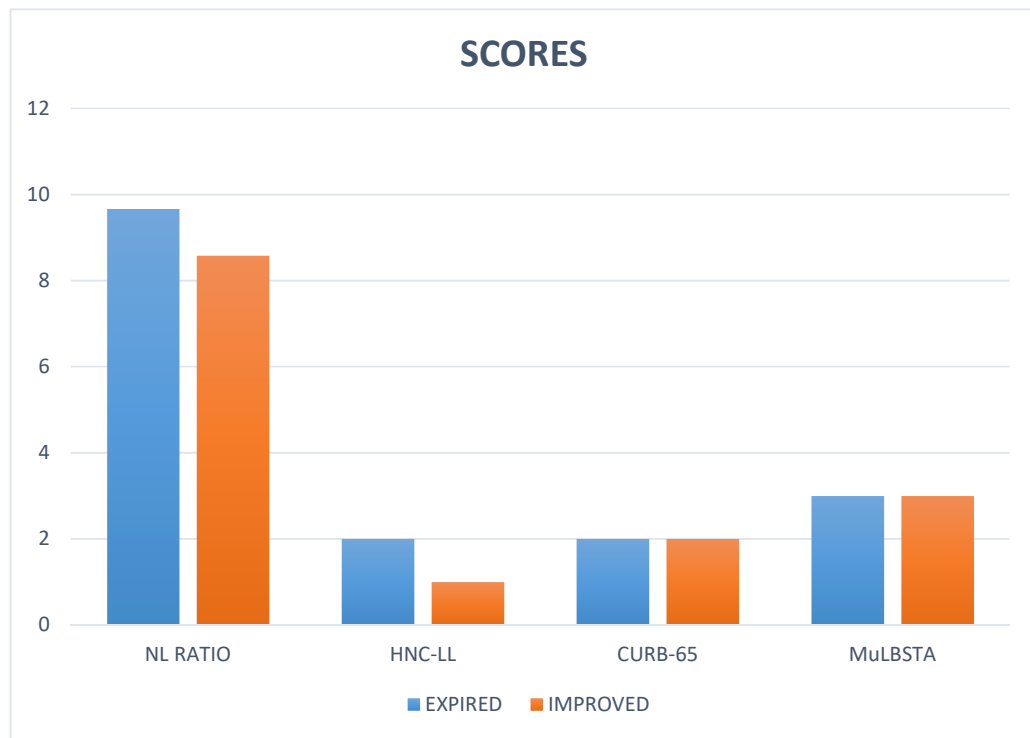
Graph 22: Distribution of patients based on COVID-19 disease outcome

Table 23: Descriptive statistics of the severity indicators of COVID-19

Variables	Sub-Category	Outcome		p-value
		Expired	Improved	
NL ratio	Median (IQR)	9.67 (11.63)	8.58 (14.65)	0.3241 [#]
HNC-LL score	Median (IQR)	2 (1.6)	1 (1.4)	0.3124 [#]
CURB-65	Median (IQR)	2 (1.5)	2 (2.4)	0.7562 [#]
MuLBSTA	Median (IQR)	3 (3.2)	3 (3.3)	0.0632[#]

#-Mann Whitney U test

The NL ratio ranged from 0 to 79.33, with a mean \pm SD of 12.14 ± 11.73 and median of 9.12. The median and IQR of expired and improved groups were 9.67 (11.63) and 8.58 (14.65) ($p=0.3241$) respectively. The mean \pm SD and median (range) of HNC-LL score were 3.34 ± 1 and 4 (0-5), respectively. The median and IQR of expired and improved groups were 2 (1.6) and 1 (1.4) ($p=0.3124$) respectively. The mean \pm SD and median (range) of MuLBSTA were 2.78 ± 0.93 and 3 (1-6), respectively. The median and IQR of expired and improved groups were 3 (3.2) and 3 (3.3) ($p=0.0632$) respectively. The mean \pm SD and median (range) of CURB-65 were 1.71 ± 0.85 and 2 (0-4), respectively (Table 12). The median and IQR of expired and improved groups were 2 (1.5) and 2 (2.4) ($p=0.7562$) respectively (Table 23 and graph 23).



Graph 23: Distribution of various scoring system among expired and improved population

Table 24: Spearman’s Correlation of different parameters among overall, expired and improved COVID-19 patients

Variables	All observation		Improved		Expired	
	Correlation coefficient	p-value	Correlation coefficient	p-value	Correlation coefficient	p-value
HNC-LL & NL ratio	0.6105	< 0.001*	0.6837	< 0.001*	0.4851	< 0.001*
HNC-LL & CURB-65	0.1116	0.1861	0.0734	0.4867	0.1726	0.2306
HNC-LL & MuLBSTA	0.3034	< 0.001*	0.28399	0.0061*	0.3229	0.0222*
NL ratio & CURB 65	0.2430	0.0036*	0.2754	0.0079*	0.1795	0.2124
NL ratio & MuLBSTA	0.3054	< 0.001*	0.3471	< 0.001*	0.1792	0.2131
MuLBSTA & CURB-65	0.0854	0.312	0.0481	0.6488	0.1725	0.231
Hospital Stay & HNC-LL	0.1153	0.1716	0.2104	0.0441*	0.0234	0.8716
Hospital stay & NL ratio	0.1270	0.132	0.2495	0.0165*	-0.0196	0.8923
Hospital stay & MuLBSTA	-0.012	0.8858	0.0631	0.5502	-0.0828	0.5675
Hospital stay & CURB-65	0.0020	0.981	0.0803	0.4469	-0.1618	0.2617

** Indicates statistical significance.*

Spearman's Correlation of different parameters among patients who expired and who improved is summarized in table 24. Among the overall population, there was significant large positive correlation between HNC-LL & NL ratio (**p<0.001**), significant moderate positive correlation between HNC-LL & MuLBSTA (**p<0.001**) and NL ratio & MuLBSTA (**p<0.001**), significant small positive correlation between NL ratio & CURB-65 (**p=0.0036**). Among improved patients, there was significant large positive correlation between HNC-LL & NL ratio (**p<0.001**), significant moderate positive correlation between NL ratio & MuLBSTA (**p<0.001**), significant small positive correlation between HNC-LL & MuLBSTA (**p=0.0061**), NL ratio & CURB-65(**p=0.0079**), Hospital Stay & HNC-LL (**p=0.0441**) and Hospital stay &NL ratio (**p=0.0165**). We observed a significant moderate positive correlation between HNC-LL & NL ratio (**p<0.001**) and HNC-LL & MuLBSTA (**p=0.0222**) in expired patients.

Table 25: Comparison of different scores with severity of disease

Variables	Severity of Disease		Total	p-value
	Not Severe	Severe		
NL ratio	8.78 ± 9.87	13.32 ± 12.14	12.14 ± 11.73	0.0011^{MW*}
	4.36 (0, 36)	10.33 (0, 79.33)	9.12 (0, 79.33)	
HNC-LL score	3 ± 1.18	3.46 ± 0.91	3.34 ± 1	0.0123^{MW*}
	3 (0, 5)	4 (1, 5)	4 (0, 5)	
MuLBSTA	2.62 ± 1.04	2.84 ± 0.89	2.78 ± 0.93	0.0792 ^{MW}
	2 (1, 6)	3 (1, 5)	3 (1, 6)	
CURB-65	1.27 ± 0.8	1.87 ± 0.81	1.71 ± 0.85	<0.001^{MW*}
	1 (0, 3)	2 (0, 4)	2 (0, 4)	

*MW – Mann Whitney U test, * indicates statistical significance.*

Mann Whitney U test showed a significant difference in distribution of NL ratio ($p=0.0011$), HNC-LL ($p=0.0123$) and CURB-65 ($p<0.001$) with the severity of disease. However, there is no significant difference in the distribution of MuLBSTA with the severity of disease. Table 25 summarizes the comparison of different scores with severity of disease.

Table 26: Spearman's Correlation of different parameters among patients with and without severe condition

Variables	Severe		Not Severe	
	Correlation coefficient	p-value	Correlation coefficient	p-value
HNC-LL & NL ratio	0.5051	< 0.001*	0.7713	< 0.001*
HNC-LL & CURB-65	0.0496	0.6155	0.0693	0.6835
HNC-LL & MuLBSTA	0.1855	0.0582	0.4674	0.0035*
NL ratio & CURB-65	0.1654	0.09185	0.2183	0.1942
NL ratio & MuLBSTA	0.2020	0.0387*	0.4353	0.0071*
MuLBSTA & CURB-65	-0.0048	0.9613	0.1414	0.404
Hospital Stay & HNC-LL	0.1246	0.2053	-0.0284	0.8674
Hospital stay & NL ratio	0.1564	0.111	-0.01868	0.9126
Hospital stay & MuLBSTA	-0.0817	0.4073	0.1647	0.3299
Hospital stay & CURB-65	-0.01996	0.8398	0.05129	0.763

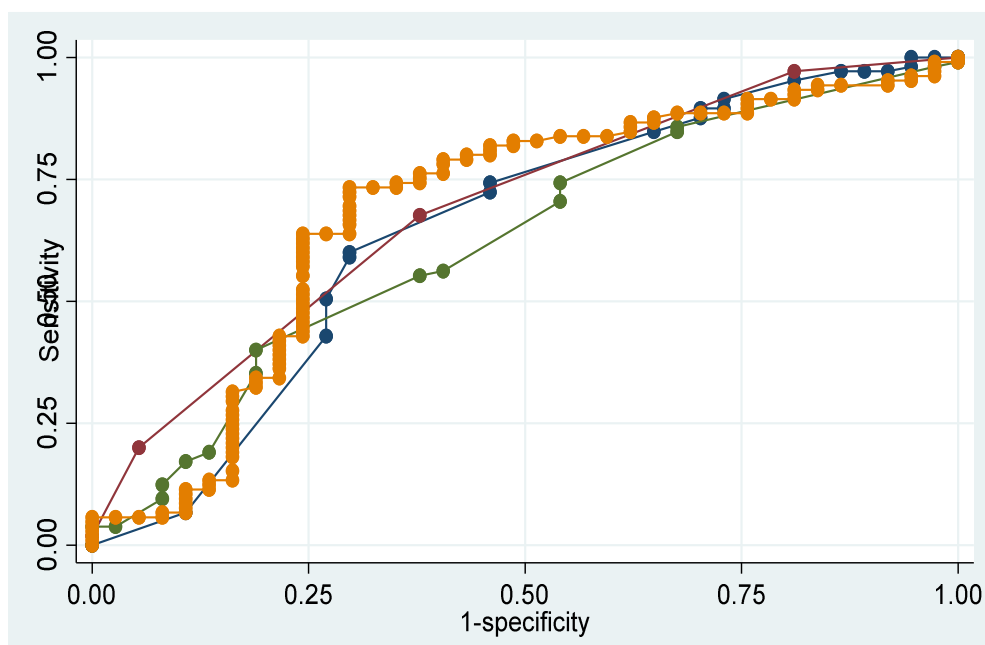
* Indicates statistical significance.

Table 26 summarizes the spearman's correlation of HNC-LL, NL ratio, MuLBSTA, CURB-65 and Hospital stay among patients with and without severe condition. Spearman's correlation test showed a significant moderate positive correlation between HNC-LL & NL ratio ($p < \mathbf{0.001}$) and low positive correlation between NL ratio & MuLBSTA ($p = \mathbf{0.0387}$) among the patients with severe condition. Among the patients without severe disease, we observed a significantly large positive correlation between HNC-LL & NL ratio ($p < \mathbf{0.001}$), significant moderate positive correlation between HNC-LL & MuLBSTA ($p = \mathbf{0.0035}$) and NL ratio & MuLBSTA ($p = \mathbf{0.0071}$).

Table 27: Optimal cut-off and accuracy indices of HNC-LL score in predicting severity in COVID-19 patients

	N	AU-ROC	Std. error	[95% conf. interval]		P value
HNC-LL SCORE	142	0.6477	0.0577	0.53462	0.76087	0.5191
CURB-65	142	0.6907	0.0477	0.59721	0.78425	
MuLBSTA	142	0.6263	0.0543	0.51982	0.73269	
NLR RANGE	142	0.6842	0.0564	0.57363	0.79471	

Table 27 summarizes the optimal cut-off and accuracy indices of HNC-LL score in predicting severity in COVID-19 patients. The AUC for HNC-LL score is 0.75 (95% CI: 0.53462-0.76087) at cut-off > 2.5 (Graph 24).

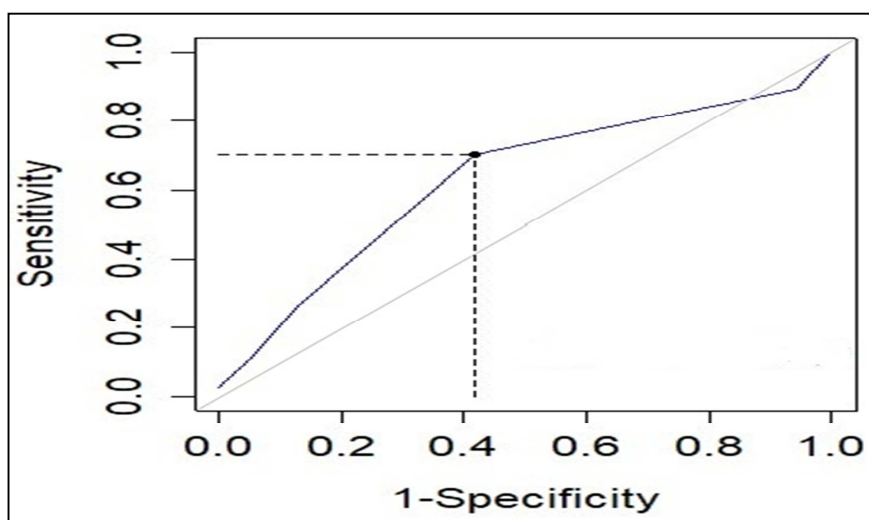


Graph 24: ROC curves for HNC-LL score in predicting severity in COVID-19 patients

Table 28: Optimal cut-off and accuracy indices of HNC-LL score in predicting severity in COVID-19 patients

Variable	HNC-LL score
Cut off	(>) 3
AU-ROC (95% CI)	0.63 (0.523, 0.737)
Sensitivity (95% CI)	70.27% (53.02% - 84.13%)
Specificity (95% CI)	58.1% (48.07% - 67.66)
PPV (95% CI)	37.14% (28.29% - 56.99%)
NPV (95% CI)	84.72% (72.59% - 89.32%)
LR +	1.68 (1.23 - 2.28)
LR-	0.51 (0.30 - 0.86)
Odds Ratio (95% CI)	1.56 (1.08 - 2.28)
p-value	0.0197 *

**Indicates statistical significance*



Graph 25: ROC curves for HNC-LL score in predicting severity in COVID-19 patients

DISCUSSION

SARS-CoV-2 causing COVID-19 infection is a rapidly evolving virus with various disease related implications. It has varying clinical presentation, ranging from asymptomatic disease to severe disease. The present study was conducted to evaluate the role of HNC-LL score as an early predictor of severity of COVID-19 among 142 patients diagnosed with COVID-19. Compared to the previous studies by Zhou F, et al¹³, Liu K, et al⁵⁹, Huang C, et al⁶⁰, Cao J, et al⁶¹ and Giacomelli A, et al⁶² that reported 11.7 to 28.2% mortality rate among COVID-19 patients, higher mortality rate was reported in our study (35.2%). The variation could be due to heterogeneity of study population, time of consultation, treatment strategies and availability of resources for thorough management.

The patients belonged to the age group of 25 to 91 years with majority being over 40 years of age. The median and mean age was 55 years and 55.67 years, respectively. The age distribution was consistent with previous studies by Wang D, et al⁶³ and Baloch S, et al⁶⁴ which showed that the median age was 45 to 56 years. In our study, older age was significantly associated with higher mortality. This was in accordance with the previous studies which showed that case fatality rate (CFR) increased and increasing age of 18% CFR among patients over 80 years⁶⁵. This could be due to the underlying comorbidities and related immunocompromised state of the patients with declined immune function, which can be easily triggered by viral infections⁶⁶.

Our study population comprised of males predominantly (78%) which was consistent with a study by Taj S, et al⁶⁷. Previous studies suggested that severity of COVID-19 infection was higher in males than females⁶⁸. Although previous studies have suggested a strong link between male patients with comorbidities and mortality, but in our study, similar link was not observed⁴⁹. The most common reported symptom was breathlessness (68.3%), followed by fever (56.3%), cough (45.1%), myalgia (28.2%) and loss of taste (2.8%) which was in accordance with the previously published literature^{69,70}. Respiratory failure is one of the major causes of mortality in COVID-19 patients⁷¹. Oxygen therapy is the essential treatment step in majority of cases, particularly severe disease. In our study, majority of the patients were on room air (45.1), (41.6%) were on oxygen mask which was similar between improved and expired patients.

Considering that, COVID-19 primarily affects the respiratory system, previous studies had suggested decreased oxygen saturation levels, lower RR and the ratio of oxygen saturation and fraction of inhaled oxygen at admission and at the time of exacerbation as the predictors of mortality^{49,72}. In our study, no significant difference was observed in RR and SpO₂ between groups. Among the important inflammatory markers deemed significant in literature^{36,37}, we evaluated ferritin, LDH, hs-CRP, IL-6 levels and PCT. Mean LDH, hs-CRP and IL-6 levels were significantly higher among the expired patients compared to improved patients suggestive of higher inflammatory response in severe COVID-19 infection, poor disease control and increased risk of respiratory distress.

Across many studies, various hematological, coagulation and biochemical biomarkers are being considered as a predictor of severity and outcome of COVID-19 infection^{7,35,39}. However, in this study all hematological, biochemical and coagulation parameters were not significant between improved and expired groups ($p > 0.05$)^{38,73}.

Although several independent risk factors or predictors of mortality secondary to COVID-19 disease have been identified. The need for the hour is to develop a prognostic scoring system based on clinical and laboratory markers to predict the disease prognosis. Having a risk prediction model with scoring system at the beginning of patient visit at earlier stages or at admission will be beneficial. This model will help grade patients based on severity into mild, moderate or high risk of mortality or poor prognosis and identify potentially high-risk patients. Risk prediction models take into account the demographics, medical history, clinical and readily available laboratory parameters at admission. In our study, we have used NLR, MuLBSTA, CURB-65 and HNC-LL to assess the mortality risk.

NLR is an inflammatory marker used to predict the prognosis of various diseases such as cancer, cardiovascular diseases, infections and sepsis⁷⁴. This marker is a quick and easy predictor of disease prognosis and is positively related to severity of disease, higher levels indicate poor prognosis^{75,76}. Higher NLR values during the first 14 days of COVID-19 disease are ought to be related to poor prognosis⁷⁷. Previous studies have demonstrated elevated neutrophil to lymphocyte ratio as independent predictor of disease severity and mortality in COVID-19 patients and the cut off value of 3.13 for NLR is used to assess severity^{50,78}. In our study, the NLR ranged from 0 to 79.33, with a mean 12.14 and median of 9.12. However, the mean NLR among improved and expired patients was not significant.

The MuLBSTA scoring system was widely used as an early warning model to predict mortality in viral pneumonias. It was originally developed and validated by Guo L, et al. By using a 12-point cut off value, MuLBSTA scoring was 78% sensitive and specific in identifying 90-day in hospital mortality among Viral pneumonia patients⁴⁴. In another study, using a cut off value of 5 points and 11 points, Iijima Y, et al⁵² reported 100% and 83.3% sensitivity, respectively and 34.5% and 71.4% specificity, respectively among COVID-19 patients. In our study, mean score was 2.78 and based on MuLBSTA score, 41.6% had mild disease and only 2% had severe disease. Severity of COVID-19 patients based on MuLBSTA score was also not significant between expired and improved patients.

Although the indices used in MuLBSTA system including multilobular infiltration, lymphocyte count, bacterial infection, history of smoking, hypertension and age are readily available at the time of admission, making this an easier scoring system for pneumonia; however, the presence of bacterial coinfection is difficult to appreciate clinically in COVID-19 as most patients have characteristic dry cough. Hence, a modified scoring system for COVID-19 severity can be used in future studies.

The CURB-65 score is another most commonly used predictor of disease severity and mortality among patients with CAP with accurate results. Previous studies by Fan G, et al⁷⁹, Satici C, et al⁸ and Artero A, et al⁸⁰ have reported superior performance of CURB-65 score in predicting COVID-19 associated mortality with an AUC of 0.85 and 0.88, 0.82, respectively. Satici C, et al⁸ reported a 73% sensitivity and 85% specificity of CURB-65 ≥ 2 score in predicting 30-day mortality among

pediatric patients in Turkey. Zhou F et al¹³ reported significantly higher CURB-65 score among diseased patients compared to survivors.

In our study, based on CURB-65 score, 83.8% patients were categorized as mild severity (score 0-2), among them 34.5% patients died. Among 16.2% patients were categorized as moderate COVID-19(score 3-4), of which 39.1% patients died suggesting that, there was no significant difference between expired and improved patients. Olivia A, et al⁵⁴ suggested that adding hypoalbuminemia to the CURB-65 increased the predictive value of in-hospital mortality (AUC=0.905) compared to CURB-65 and CALL scores. Future studies are warranted to use this modified CURB-65 score to better predict the in-hospital mortality among COVID-19 patients.

Xiao LS, et al³ first developed the HNC-LL model consisting of indices such as hypertension, neutrophil count, C-reactive protein, lymphocyte count, lactate dehydrogenase to predict severity of COVID-19. In their study optimum cut off value of -1.508 was derived to categorize severity and based on this, patients were categorized as high risk despite the mild to moderate COVID-19 symptoms were advised to be considered for active treatment. In our study, the overall mean HNC-LL score was 3.34 and 16.9%, 76.1% and 7.04% patients were graded as mild, moderate and severe disease. We did not observe a significant difference in the mean HNC-LL scores between expired and improved patients. Additionally, severity of COVID-19 patients based on HNC-LL score was also not significant between groups. With a cut off value of >2.5 point score, the AUC of HNC-LL score 0.75 in predicting disease severity with 95% CI of 0.53-0.76.

Previous study by Xiao LS, et al³ showed superior performance of HNC-LL in predicting disease severity compared to other models such as NLR and MuLBSTA. Spearman's Correlation was used to assess the relationship between different scoring systems. Among the overall population, there was significant large positive correlation between HNC-LL & NLR ($p < 0.001$), significant moderate positive correlation between HNC-LL & MuLBSTA ($p < 0.001$) and NLR & MuLBSTA ($p < 0.001$), significant small positive correlation between NL ratio & CURB-65 ($p = 0.0036$). Among expired patients' group, there was a significant moderate positive correlation between HNC-LL & NLR ($p < 0.001$) and HNC-LL & MuLBSTA ($p = 0.0222$). We also observed significant difference in the distribution of patients based on severity between different scoring systems. This could be due to the varying indices including demographics, clinical features and different laboratory markers used in the prediction models.

Limitations of the study

- This was a single centric observational study with small sample size.
- All patients of ward and ICU were included without distinction.

Future perspectives

- Future studies are warranted utilizing the predictive models at the time of admission to predict ICU admission and management among COVID-19 patients.

SUMMARY

The present observational study was conducted in 142 adult patients with a RT-PCR or RAT confirmed COVID-19 diagnosis at KLES Dr. Prabhakar Kore Hospital to evaluate the role of HNC-LL score as an early predictor of COVID-19 severity and for further comparison of its effectiveness with known severity predictors such as CURB-65, MuLBSTA, and NLR. Ethical approval and informed consent were obtained prior to the study. Data was analyzed using statistical software R and Microsoft Excel.

Patients' demographics, detailed history of patients and respiratory parameters like respiratory rate and oxygen saturation were recorded. Blood was investigated for hematological, inflammatory, coagulation and biochemical markers. HRCT thorax was also done. By using these investigations, disease severity indexes like CURB-65, MuLBSTA, NLR and HNC-LL were calculated. These indices were used to categorize severity of COVID-19 infection.

Based on outcome, patients were categorized into improved or expired and based on severity as severe or non-severe COVID-19 infection. Disease progression was monitored in terms of duration of hospital stay. Comparison of demographics, respiratory parameters, blood biomarkers and disease outcome were assessed. Similarly, comparison of disease severity based on MuLBSTA, NLR, CURB-65 and HNC-LL and disease outcome was compared. The optimum cut off value for HNC-LL, for disease severity and outcome was estimated. Sensitivity and specificity of HNC-LL in predicting the severity of COVID -19 was analyzed.

Patients belonged to the age group of 25 to 91 years with a mean age of 55.67 years. Majority of the study population comprised of males (78.17%). The mean duration of hospital stay was significantly longer in patients who had an improvement in the disease compared to patients who succumbed ($p=0.0024$). While there was no significant difference in the outcome between genders, there was significant difference in outcome based on age ($p=0.0386$). Among the comparison of symptoms, incidence of myalgia and cough was significantly higher in improved patients. There was no significant difference in oxygen modality used between two groups.

No significant difference in mean RR and median SpO₂ was observed between expired vs improved patients. In addition, no significant difference in the mean levels of hemoglobin, total & differential leucocyte count and platelet count was observed between expired and improved patients. The mean value of liver function test and renal function test were comparable between expired and improved patients.

Significant increase in the mean value of serum inflammatory markers namely- LDH, hs-CRP, IL-6 and PCT was observed among expired patients than improved patients.

The median NL ratio, HNC-LL score, CURB-65 and MuLBSTA between expired and improved groups were comparable.

Among the overall study population and improved patients, there was significant positive correlation between HNC-LL & NL ratio, HNC-LL & MuLBSTA, NL ratio & MuLBSTA, hospital stay & HNC-LL and hospital stay and NL ratio & CURB-65 ($p<0.05$). A significant moderate positive correlation was observed between HNC-LL & NL ratio ($p<0.001$) and HNC-LL & MuLBSTA ($p=0.0222$) in expired patients.

We observed a significant difference in distribution of NL ratio ($p=0.0011$), HNC-LL ($p=0.0123$) and CURB-65 ($p<0.001$) with the severity of disease. The AUC for HNC-LL score is 0.75(95% CI: 0.534-0.760) at cut-off > 2.5 .

Thus, laboratory parameters such as LDH, IL-6, hs-CRP and disease severity scores namely- NLR, CURB-65 and HNC-LL predict severity of disease and mortality risk among COVID-19 patients.

CONCLUSION

In our study, laboratory parameters such as LDH, IL-6, hs-CRP were significant in patients with severe COVID-19 infection. NLR, MuLBSTA, CURB-65 and HNC-LL scores were used to predict disease severity and mortality risk among COVID-19 patients. We observed a significant difference in the predictive scores of CURB-65, NLR and HNC-LL between patients with severe and non-severe COVID-19 infection. Early identification of patients with severe COVID-19 followed by early interventions are beneficial in saving lives. A quick and accurate assessment of mortality risk allows the clinician to triage and optimize the right care for patients with highest risk, particularly in a resource-poor setting. We conclude that the novel scoring system HNC-LL can be used as a predictive marker of COVID-19 severity.

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ANNEXURE I – CONSENT FORM

INFORMED CONSENT

Dear Mr./Mrs./Dr. _____, you are kindly requested to enroll yourself in a research study titled “**HNC-LL AS A POTENTIAL SCORE FOR PREDICTING SEVERITY IN COVID-19 PATIENTS**”- **ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY** being conducted by _____, a post graduate student in M.D. General Medicine and the study will be carried out under the direct supervision and guidance of Dr. ARIF MALDAR, Associate Professor, Department of General Medicine, Jawaharlal Nehru Medical College, Belagavi.

You have been requested to participate in this as you fit into the laid out criteria for a study ‘subject’/ participant.

Your participation in study is voluntary. During the study you will be asked some questions and you are supposed to answer to the best of your knowledge. Your decision whether or not to participate in the study will not affect your treatment in any form. If you decide to participate you are free to withdraw at any time.

TITLE OF THE STUDY:

“HNC-LL AS A POTENTIAL SCORE FOR PREDICTING SEVERITY IN COVID-19 PATIENTS - ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY.

PURPOSE OF THE STUDY:

To calculate HNC-LL score for predicting severity in COVID-19 patients and compare with other pre-existing scores.

PROCEDURES INVOLVED:

If you agree to enroll yourself in my study, you will be interviewed regarding your present, past and family history then you will be clinically examined in detail and investigated accordingly.

1. HRCT Thorax.
2. CBC
3. LFT (AST, ALT, AG Ratio)
4. BUN, Creatinine
5. Serum electrolytes.
6. hsCRP, Serum ferritin, LDH, D-dimer, IL-6.
7. PT Ratio /INR.
8. HRCT Thorax
9. Sr.PCT

RISKS AND BENEFITS:

There are no potential risks involved in this study.

Benefits of taking part in this research:

By taking part in this study, clinical features, laboratory findings can be understood and mortality of patients can be predicted early in the disease.

VOLUNTARY PARTICIPATION / WITHDRAWAL FROM THE STUDY:

Taking part in the study is voluntary. You may choose not to enroll yourself in this study and may choose to leave the study anytime in between.

ALTERNATIVES:

Your decision regarding participation in study will not change the present or future health care services offered to you at KLES Dr.Prabhakar Kore Hospital and Medical Research Centre, Belagavi. You would simply be excluded from the study if you wish to, and all your details shall be kept confidential and you will get the routine line of management.

PRIVACY AND CONFIDENTIALITY:

All data collected or disclosed by you during the course of participation of study, will be kept fully confidential. If however during the course it becomes necessary for the progress of the course to disclose the identity, it would be done so only after your informed & written consent.

The only people to know that you are a research subject are members of the research team. No information about you will be disclosed to other without your written permission except:

- In an emergency to protect your rights AND welfare.
- If required by law.

AUTHORIZATION TO PUBLISH RESULT:

The results of the study may be used to publish an article. When the results of research published or discussed, in a conference, no information will be displayed that would disclose your identity. Any information obtained in connection with this study and that can be identified with you will remain confidential.

FINANCIAL INCENTIVES FOR PARTICIPATION:

No additional costs shall be incurred upon you for the purpose of this study.

It is purely being done with the idea of research and all the cost of study will be borne by the investigator.

COMPENSATION:

In the event that you become injured as a result of taking part in this study, treatment will be offered to you at KLES Dr.Prabhakar Kore Hospital and Medical Research Centre, Belagavi, or you will be given information about where to receive medical care. However, no reimbursement, compensation or free medical care will be given.

Authorization to publish the results:

The results of the study would be forwarded to the KLE University, Belagavi as part of requirement towards the completion of MD degree, review and publication.

In case of the queries during study or in future you may contact following persons

1. **Dr. HARSHA HEGDE CHAIRPERSON, JNMC**, Institutional Ethics
Committee on Human Subject Research Belagavi- 9480422500

CONSENT FORM

I voluntarily agree to take part in this study by signing below. I may withdraw at any time. I am not giving up any of my legal rights by signing this form. My signature below indicates that I have read this consent form, or it has been read to me, this consent form and have had all the questions answered

Signature / Left Thumb print of the Participant or legally authorized representative

Participant's name:.....

Signature / Left thumb impression:

of the participant

Name of the legally authorized

representative / guardian

Signature / Left thumb impression :.....

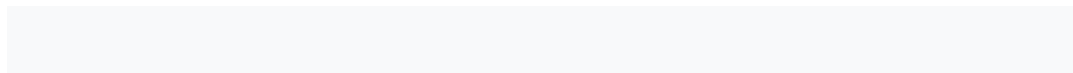
Witness' name

Signature / Left thumb impression

Investigator's name and signature

Date:

PLACE:



ANNEXURE- II

PROFORMA

CASE NO:

NAME:

AGE/SEX:

IP NO.:

ADDRESS:

OCCUPATION

COMPLAINTS AT PRESENTATION:

Past history:

Family history

Personal history

Smoking History -- Yes/ No.

Treatment history

PHYSICAL EXAMINATION:

GENERAL CONDITION:

PALLOR- YES/NO

ICTERUS-YES/NO

LYMPHADENOPATHY-YES/NO

CYANOSIS- YES/NO

CLUBBING-YES/NO

EDEMA-YES/NO

VITALS:

TEMPERATURE :

PULSE :

BLOOD PRESSURE :

RESPIRATORY RATE :

SYSTEMIC EXAMINATION:

C.V.S.-

R.S.-

P.A.-

C.N.S.-

OUTCOME OF THE PATIENT

1. Improved
2. Recovered
3. Mortality

SEVERITY OF THE COVID19 INFECTION

SPO2 <93%

RESPIRATORY FAILURE

SHOCK

MULTIORGAN DYSFUNCTION

INVESTIGATIONS:

SERUM FERRITIN - D-Dimer IL-6 SR. FERRITIN SR.PROCALCITONIN	HRCT THORAX CORADS SEVERITY SCORE Multilobular involvement of Lungs
HB - WBC – Platelet count- Neutrophils - Lymphocytes - Monocytes - Eosinophils - Basophils – ABSOLUTE Neutrophil count -- ABSOLUTE Lymphocyte count --	T.BILIRUBIN - SGOT - SGPT - A/ G Ratio PT - control- test - INR – Serum Creatinine – Blood Urea - Sodium- Potassium- Chloride - Lactate dehydrogenase(LDH) HSCRIP

ANNEXURE III

MASTER CHART

SL NO	IP No	Date of Admission	date of discharge	#NAME? stay in hospital	Age	MULBSTA AGE > 60	CURB 65 AGE > 65	Sex	Symptoms (C-cough; F-fever; B-breathlessness; N-Myalgia, Loss of smell/L; Loss of taste-LT)	Any other symptoms	CLINICAL PARAMETERS AT Admission																												outcome																	
											Admission SpO2	Admission respiratory rate (RR/min)	CURB 65 RESP > 30	BP	CURB 65 BP < 90	HNCL BP > 140/90MMHG	Admission SpO2	SpO2 > 93 AT ROOM AIR	Admission O2 mobility (O2 mask, RBM, HFO, NIV, Ventilator)	SEVERE DISEASE	Co-morbidities	HYPERTENSION HISTORY	CT severity score (-/25)	MULBSTA MULTILOBRE INFILTRATE	HEMOGLOBIN	TLC	NEUTROPHIL %	ANC 10^3 X /MICROL	HNCL ANC > 6.3	Lymphocyte % 1	ALC	MULBSTA ALC < 0.8/L	HNCL ALC < 1.1	Platelets	Ferritin	LDH	HNCL LDH > 245U/L	ICOP (value)		HNCL HSEPR > 10MG/L	IL-6	d-Dimer	Bilirubin	SGOT	SGPT	AG RATIO	Urea	CURB 65 UREA > 7MMOL/L	Creatinine	CNS-CONFUSED - YES / NO	SMOKING HISTORY - YES / NO	SR PCT	MULBSTA BACTERIAL INFECTION	HNCL SCORE	MULBSTA	NLR RANGE 0.78 TO 3.53
1	1051210	01 May 2021	22 May 2021	#NAME? 37	0	0	0	Male	FBM		34	1	130/80	0	0	93%	YES	NIV	1	NONE	0	4	5	14.1	12.1	87	10.4	1.035	8	1	0	1.237	124	766	236	0	57.5	1.419	221	518	1.25	17	17	1.6	29	1	0.75	0	0	0.25	0	1.266	5	10.4	2	improved
2	1051644	06 May 2021	15 May 2021	#NAME? 43	0	0	0	Male	FM		43	1	80/50	1	0	93%	NO	RA	0	DM HTN IHD	2	14	5	14.5	12.7	88	11.2	1.035	7	0.8	4	1.237	267	296	1538	1.066	36.4	1.419	22	1417	2	759	522	0.8	62	1	0.15	0	0	0.51	4	2.332	15	14.0	3	improved
3	1051255	02 May 2021	15 May 2021	#NAME? 35	0	0	0	Male	B		28	0	140/60	1	0.969	62%	YES	RA	1	NONE	0	6	5	8.7	21.5	93	20	1.035	5	1	0	1.237	143	96	1184	1.066	135.7	1.419	86	5000	0.49	32	65	1	64	1	0.89	0	0	0.1	0	3.301	5	20.0	2	expired
4	1051522	05 May 2021	13 May 2021	#NAME? 44	0	0	0	Male	BC		44	1	130/90	0	0	67%	YES	RA	1	NONE	0	22	5	14	13.1	67	8.8	1.035	9	1.2	0	0	160	749	655	1.066	274	1.419	45	943	0.62	41	55	1	64	1	0.75	0	0	0.17	0	1.095	5	17.3	1	expired
5	1051477	04 May 2021	15 May 2021	#NAME? 75	2	1	0	Male	B		60	1	110/70	0	0	86%	YES	RBM	1	HTN	2	17	5	12.2	3.8	87	3.3	0	6	0.2	4	1.237	113	653	808	1.066	226	1.419	23	1026	0.41	73	22	1.2	81	1	1.31	0	2	2.5	4	1.297	19	16.5	3	expired
6	1051836	08 May 2021	21 May 2021	#NAME? 54	0	0	0	Female	FM		24	0	200/100	0	0.969	57%	YES	RA	1	NONE	0	16	5	12.1	21.6	92	19.9	1.035	4	0.9	0	1.237	290	441	957	1.066	102	1.419	20	1378	0.35	40	15	1	73	1	1.01	0	0	2.2	4	3.301	9	22.1	1	improved
7	1051823	08 May 2021	21 May 2021	#NAME? 38	0	0	0	Female	LT.M	VOMITING	29	0	120/70	0	0	75%	YES	O2 MASK	1	NONE	0	17	5	14.2	8.6	91	7.8	1.035	7	0.6	4	1.237	217	1032	662	1.066	131	1.419	183	1431	0.4	59	40	1.2	27	1	0.68	0	0	1.9	4	2.332	13	13.0	1	improved
8	1051635	06 May 2021	10 May 2021	#NAME? 60	0	0	0	Male	FBC		40	1	90/50	1	0	90%	YES	RA	1	NONE	0	16	5	11.9	5.1	90	4.7	0	7	0.3	4	1.237	108	1430	225	0	29	1.419	48	452	0.31	48	30	1	72	1	1.66	0	0	1.3	4	0.231	13	15.7	3	improved
9	1051731	06 May 2021	18 May 2021	#NAME? 51	0	0	0	Male	CB		28	0	100/60	1	0	78%	YES	O2 MASK	1	HTN DM	2	9	5	14.4	17.3	95	16.5	1.035	4	0.6	4	1.237	230	585	552	1.066	114	1.419	22	377	0.67	65	48	1.2	47	1	0.68	1	0	0.3	0	2.332	11	27.5	3	improved
10	1051610	05 May 2021	18 May 2021	#NAME? 49	0	0	0	Female	B	Diarrhoea	49	1	130/90	0	0	80%	YES	O2 MASK	1	NONE	0	6	5	15.8	15	94	14	1.035	4	0.7	4	1.237	240	742	339	1.066	150	1.419	46	1416	0.48	22	24	1.5	57	1	0.81	0	0	0.1	0	2.332	9	20.0	2	improved
11	1050024	20 April 2021	14 May 2021	#NAME? 26	0	0	0	Male	FB	Diarrhoea	39	1	120/80	0	0	68%	YES	RA	1	NONE	0	17	5	13.9	11.4	89	10.2	1.035	8	0.9	0	1.237	194	676	608	1.066	114	1.419	94	4292	0.27	65	68	1.7	32	1	1	0	2	0.3	0	2.332	7	11.0	2	improved
12	1051827	08 May 2021	17 May 2021	#NAME? 57	0	0	0	Male	BFM		24	0	110/70	0	0	88%	YES	RA	1	NONE	0	21	5	11.1	12.9	83	10.6	1.035	11	1.4	0	0	398	3063	1171	1.066	5.7	0	65	1503	1.06	767	630	1.2	47	1	0.65	0	0	0.29	0	-0.324	5	7.6	1	improved
13	1051963	09 May 2021	21 May 2021	#NAME? 30	0	0	0	Male	B		46	1	120/80	0	0	60%	YES	RBM	1	NONE	0	22	5	15.6	10.6	83	8.8	1.035	7	0.7	4	1.237	274	674	160	0	15.1	1.419	36	1252	0.75	35	44	1.1	58	1	0.91	0	0	0.05	0	1.266	9	12.6	2	improved
14	1051952	09 May 2021	21 May 2021	#NAME? 36	0	0	0	Male	F		46	1	110/70	0	0	91%	YES	RBM	1	NONE	0	24	5	11.5	14.2	88	12.5	1.035	6	0.8	4	1.237	287	1402	622	1.066	76.6	1.419	84.9	437	0.21	33	22	1.4	41	1	0.93	0	0	0.09	0	2.332	9	15.6	2	improved
15	1051902	08 May 2021	21 May 2021	#NAME? 88	2	1	0	Female	B		36	1	150/80	0	0.969	51%	YES	RA	1	DM HTN HYPOTHYROIDISM	2	21	5	9.5	6.5	86	5.7	0	13	0.8	4	1.237	152	8957	468	1.066	36.6	1.419	626	1344	0.39	103	13	1	41	1	1.32	1	2	34.4	4	2.266	19	7.1	4	expired
16	1051674	06 May 2021	11 May 2021	#NAME? 55	0	0	0	Male	BC		48	1	120/80	0	0	75%	YES	NIV	1	DM	0	15	5	12.4	3.1	55	1.7	0	36	1.1	0	1.237	174	925	561	1.066	160	1.419	44	318	0.37	105	38	1.2	30	1	1.24	0	0	0.1	0	1.297	5	1.5	2	improved
17	1051496	04 May 2021	10 May 2021	#NAME? 74	2	1	0	Male	M		20	0	130/80	0	0	88%	YES	O2 MASK	1	NONE	0	17	5	12.5	12.8	75	9.6	1.035	8	1	0	1.237	295	1511	402	1.066	152	1.419	35	559	1.67	45	86	1.4	43	1	0.93	0	0	0.12	0	2.332	7	9.6	2	improved
18	1050836	27 April 2021	11 May 2021	#NAME? 65	2	1	0	Female	B		20	0	110/80	0	0	95%	YES	O2 MASK	1	NONE	0	16	5	8.6	4.1	77	3.1	0	19	0.8	4	1.237	62	591	314	1.066	176	1.419	20.11	573	0.73	10	31	1.3	20	1	0.82	0	0	0.06	0	1.297	11	3.9	2	improved
19	1050847	27 April 2021	13 May 2021	#NAME? 38	0	0	0	Male	B		24	0	120/70	0	0	73%	YES	RBM	1	NONE	0	21	5	13.4	14.4	90	12.5	1.035	2	0.3	4	1.237	232	718	664	1.066	109	1.419	26	1530	0.37	22	27	1.2	42	1	0.72	0	0	0.04	0	2.332	9	41.7	1	improved
20	1051811	07 May 2021	22 May 2021	#NAME? 52	0	0	0	Male	MBF		20	0	100/80	0	0	88%	YES	RBM	1	NONE	0	18	5	14.7	7.2	84	6.1	0	11	0.8	4	1.237	89	1966	348	1.066	107	1.419	3.65	609	1.1	55	44	1.1	26	1	0.73	0	3	0.11	0	1.297	12	7.6	1	improved
21	1051866	08 May 2021	25 May 2021	#NAME? 56	0	0	0	Female	M	throatpain	26	0	110/90	0	0	85%	YES	O2 MASK	1	NONE	0	12	5	11.6	17.9	88	15.8	1.035	4	0.8	4	1.237	201	363	619	1.066	140	1.419	42	308	0.33	58	61	0.9	46	1	0.8	0	3	0.47	0	2.332	12	19.8	1	improved
22	1051799	07 May 2021	22 May 2021	#NAME? 52	0	0	0	Female	B		24	0	150/90	0	0.969	93%	YES	O2 MASK	1	DM HTN HYPOTHYROIDISM	2	17	5	11.3	12.3	83	10.3	1.035	15	1.8	0	0	223	2572	978	1.066	147	1.419	286	356	0.28	38	19	1.6	46	1	0.65	0	0	0.05	0	2.064	7	5.7	1	improved
23	1051977	10 May 2021	11 May 2021	#NAME? 79	2	1	0	Male	F	Giddiness	25	0	100/70	0	0	100%	YES	VENTILATOR	1	AKI IHD HTN	2	17	5	12.4	12	85	10.2	1.035	10	1.2	0	0	224	304	1200	1.066	141	1.419	98	1454	0.35	286	146	0.8	163	1	4.66	1	0	52.4	4	1.095	13	8.5	3	improved
24	1051280	02 May 2021	30 May 2021	#NAME? 71	2	1	0	Female	CF																																															

87	1024639	04 October 2020	13 October 2020	#NAME?	44	0	0	Female	F		18	0	120/80	0	0	96%	NO	RA	0	0	13	5	13	6.8	71	4.82	0	21	1.6	0	0	235	306	404	1.066	91.2	1.419	105	448	0.52	32	24	1.1	8	0	0.49	0	2	0.4	0	0.06	7	3.4	0	improved	
88	1021845	27 August 2020	14 September 2020	#NAME?	52	0	0	Male	B		25	0	80/60	1	0	95%	YES	RBM	1	DM	0	5	5	13.8	20.4	90	18.4	1.035	5	1	0	1.237	183	210.7	660	1.066	11.5	1.419	33.51	5000	69	19	40	1	59	1	0.83	0	0	11	4	2.332	9	18.4	2	improved
89	1023488	18 September 2020	25 September 2020	#NAME?	64	2	0	Male	Cfb		26	0	160/100	0	0.969	98%	NO	RA	0	DM,HTN,CKD	2	15	5	10	9.8	91	8.9	1.035	4	0.4	4	1.237	164	2000	433	1.066	50.6	1.419	218	775	9	66	38	1.1	120	1	10.43	0	0	17.4	4	3.301	17	22.3	1	improved
90	1019426	23 July 2020	29 July 2020	#NAME?	65	2	1	Male	C, F		20	0	140/88	0	0.969	97%	NO	RA	0	DM, HTN	2	11	5	14.1	7.2	70	5	0	25	1.8	0	0	161	429	283	1.066	111.5	1.419	32.45	746	0.51	54	44	1.3	31	1	0.79	0	0	0.24	0	1.029	9	2.8	2	improved
91	1023326	16 September 2020	19 September 2020	#NAME?	85	2	1	Male	F		19	0	140/100	0	0.969	96%	NO	RA	0	DM, HTN	2	18	5	10.11	11.4	74	8.5	1.035	19	2.1	0	0	203	61.46	251	1.066	58.8	1.419	52.81	437	1.66	114	105	1.1	56	1	2.32	0	0	0.3	0	0.645	9	4.0	2	improved
92	1024174	26 September 2020	01 October 2020	#NAME?	60	0	0	Female	FB	seizures	20	0	100/60	1	0	67%	YES	RA	1	Epilepsy	0	21	5	11.4	8.1	70	5.7	0	30	2.2	0	0	25	22.4	397	1.066	5.6	0	33	472	0.13	49	22	1.1	22	1	68	0	0	0.19	0	-1.359	5	2.6	2	improved
93	1022906	10 September 2020	30 September 2020	#NAME?	78	2	1	Male	C, B		19	0	90/70	1	0	94%	YES	RBM	1	DM	0	22	5	12.8	6.6	88	5.8	0	9	0.6	4	1.237	187	510	509	1.066	84.7	1.419	8.96	5000	0.5	31	20	1.1	37	1	0.87	0	2	0.08	0	1.297	13	9.7	3	expired
94	1025516	15 October 2020	17 October 2020	#NAME?	82	2	1	Male	B		22	0	110/80	0	0	95%	YES	RBM	1	DM, HTN, IHD	2	16	5	10	7.2	85	6.1	0	11	0.8	4	1.237	150	10.7	207	0	1.8	0	40.83	864	0.45	11	18	0.9	23	1	0.83	0	0	0.6	4	-1.188	17	7.6	2	expired
95	1024333	29 September 2020	16 October 2020	#NAME?	26	0	0	Female	C, B, M		22	0	100/70	0	0	96%	YES	RA	0	NONE	0	11	5	13	5.2	53	2.7	0	28	1.9	0	0	229	151.9	168	0	0.4	0	15.2	140	0.48	17	12	1.6	17	0	0.63	0	0	0.4	0	-2.425	5	1.4	0	expired
96	1023727	21 September 2020	03 October 2020	#NAME?	60	0	0	Male	C, F		24	0	110/80	0	0	96%	NO	RA	0	DM	0	17	5	18.2	9.3	80	7.4	1.035	16	1.5	0	0	227	1152	573	1.066	42.9	1.419	40.27	1639	2.48	109	116	0.9	32	1	0.9	0	2	2.8	4	1.095	11	4.9	1	expired
97	1020944	14 August 2020	20 August 2020	#NAME?	39	0	0	Male	F, B		28	0	80/60	1	0	94%	YES	O2 MASK	1	NONE	0	19	5	14.6	7.2	73	5.3	0	20	1.4	0	0	340	2000	415	1.066	58.8	1.419	52.81	437	1.66	114	105	1.8	35	1	1.13	0	2	2.2	4	0.06	11	3.8	2	expired
98	1021397	20 August 2020	03 September 2020	#NAME?	56	0	0	Male	B		27	0	90/60	1	0	82%	YES	RBM	1	COPD	0	19	5	15.4	17.4	93	16.32	1.035	5	0.8	4	1.237	217	880	397	1.066	207.2	1.419	1.54	1519	0.75	22	66	1.7	65	1	0.9	0	3	0.29	0	2.332	12	20.4	2	expired
99	1023886	23 September 2020	30 September 2020	#NAME?	59	0	0	Male	M, B		22	0	150/90	0	0.969	97%	NO	RA	0	HTN	2	16	5	12.9	7.1	69	4.9	0	23	1.6	0	0	200	359	515	1.066	176.8	1.419	225.2	605	0.68	21	29	1.4	29	1	0.93	0	0	0.07	0	1.029	7	3.1	1	improved
100	1023858	23 September 2020	29 September 2020	#NAME?	66	2	1	Male	C, F, M, B		22	0	160/100	0	0.969	95%	YES	O2 MASK	1	DM, HTN	2	16	5	14.7	7.9	75	5.9	0	19	1.5	0	0	203	661	538	1.066	140.1	1.419	129.9	588	0.66	47	36	1.2	35	1	0.84	0	0	0.15	0	1.029	9	3.9	2	improved
101	1022372	04 September 2020	06 September 2020	#NAME?	70	2	1	Male	F		17	0	130/80	0	0	99%	YES	O2	1	DM, HTN	2	11	5	10.2	6	68	4.1	0	23	1.4	0	0	236	562	266	1.066	92.6	1.419	316.5	380	1	23	12	0.9	33	1	1.27	0	0	0.63	4	0.06	13	2.9	2	improved
102	1023275	15 September 2020	21 September 2020	#NAME?	75	2	1	Male	Fever		29	0	150/90	0	0.969	90%	YES	RA	1	DM, HTN	2	11	5	11	6.6	66	4.4	0	30	2	0	0	224	107.8	301	1.066	134.6	1.419	360	5000	0.54	17	13	0.8	32	1	0.96	0	0	0.2	0	1.029	9	2.2	2	improved
103	1023978	25 September 2020	01 October 2020	#NAME?	45	0	0	Male	C, B		18	0	120/80	0	0	88%	YES	RA	1	NONE	0	14	5	13.7	5	73	3.6	0	18	0.9	0	1.237	235	323.7	419	1.066	345.4	1.419	16.73	478	0.4	28	17	1.2	23	1	0.57	0	3	0.1	0	1.297	8	4.0	1	expired
104	1025259	06 September 2020	14 September 2020	#NAME?	49	0	0	Male	C, B	WEAKNESS	22	0	100/80	0	0	99%	NO	RA	0	DM	0	17	5	14.8	4.9	49	24	1.035	42	2.1	0	0	229	80	358	1.066	49.5	1.419	71.81	996	0.45	32	31	1.3	31	1	0.88	0	0	0.22	0	1.095	5	11.4	1	expired
105	1021328	19 August 2020	22 August 2020	#NAME?	34Y	2	1	Male	CF		17	0	130/80	0	0	66%	YES	RA	1	NONE	0	11	5	12.1	10.6	89	9.4	1.035	6	0.7	0	1.237	195	173	629	1.066	143.7	1.419	26.21	1592	0.45	31	36	1.7	45	1	0.76	0	0	26	4	2.332	15	13.4	2	expired
106	1047871	05 April 2021	12 April 2021	#NAME?	55	0	0	Female	c,f,b		28	0	150/90	0	0.969	80%	YES	RBM	1	HTN	2	14	5	9.6	21.4	90	19.3	1.035	7	1.5	0	0	371	1443	491	1.066	140.3	1.419	113.4	878	0.14	29	16	1.4	70	1	1.55	0	0	0.09	0	2.064	7	12.9	1	expired
107	1049630	18 April 2021	25 April 2021	#NAME?	38	0	0	Female	C,F		19	0	110/90	0	0	93	NO	RA	0	DM	0	4	0	12.7	12.3	86	10.6	1.035	7	0.8	4	1.237	276	210	518	1.066	65.6	1.419	135.7	349	0.28	29	26	1.2	26	1	0.6	0	3	1	4	2.332	11	13.3	1	expired
108	1050596	25 April 2021	01 May 2021	#NAME?	65	2	1	Female	C,M		24	0	150/90	0	0.969	90	YES	O2 MASK	1	DM	0	13	5	11.8	6.7	71	4.8	0	25	1.7	0	0	219	1718	678	1.066	212	1.419	50.99	1052	0.3	84	39	0.9	42	1	1.22	0	0	0.19	0	1.029	7	2.8	2	expired
109	1051160	30 April 2021	04 May 2021	#NAME?	78	2	1	Female	C,B		26	0	140/90	0	0.969	92	YES	O2 MASK	1	DM	0	6	5	13.6	16.7	93	15.6	1.035	5	0.9	0	1.237	231	449.6	782	1.066	189	1.419	429.8	822	0.53	27	52	1.2	26	1	0.89	0	0	0.28	0	3.301	7	17.3	2	expired
110	1051382	03 May 2021	07 May 2021	#NAME?	59	0	0	Male	c,f,b		28	0	130/80	0	0	95	NO	RA	0	NONE	0	22	5	13.3	5.5	76	4.2	0	18	1	0	1.237	156	1088	571	1.066	133.9	1.419	108.5	540	0.69	54	34	1.5	13	0	1.06	0	0	0.43	0	1.297	5	4.2	0	expired
111	1050677	26 April 2021	30 April 2021	#NAME?	33	0	0	Male	F,B		17	0	110/70	0	0	90	YES	O2 MASK	1	NONE	0	23	5	11.7	3.3	89	2.9	0	9	0.3	4	1.237	116	2817	1033	1.066	266.4	1.419	300	949	0.7	63	47	1.2	40	1	1.35	0	0	16	4	1.297	13	9.7	1	expired
112	1049991	20 April 2021	03 May 2021	#NAME?	62	2	0	Female	C,M,B		19	0	120/80	0	0.969	96	NO	RA	0	HTN,HYPOTHYROID,ALLERGIC BRONCHITIS	2	14	5	10.8	8.9	95	8.4	1.035	3	0.3	4	1.237	187	548	812	1.066	145.3	1.419	50.05	6520	81	25	18	1.2	17	0	0.47	0	0	0.07	0	3.301	13	28.0	0	expired
113	1051066	30 April 2021	05 May 2021	#NAME?	44	0	0	Male	F,B,M		28	0	130/90	0	0	84	YES	O2 MASK	1	DM	0	15	5	14.3	8.7	90	7.8	1.035	8	0.7	4	1.237	156	14954	589	1.066	292.5	1.419	34.76	1180	0.2	67	22	1.6	18	0	0.9	0	3	11	4	2.332	16	11.1	0	expired
114	1050812	27 April 2021	04 May 2021	#NAME?	68	2	1	Male	F,M		24	0	150/70	0	0.969	70	YES	RA	1	DM,HTN,HYPOTHYROIDISM	2	12	5	13	10.1	81	8.2	1.035	16	1.7	0	0	432	251.4	472	1.066	15.2	1.419	14.73	1383	0.2	17	12	1	50	1	0.97	0	0	0.9	4	2.064	13	4.8	2	expired
115	1050532	24 April 2021	24 April 2021	#NAME?	32	0	0	Male	F,M		23	0	110/80	0																																										